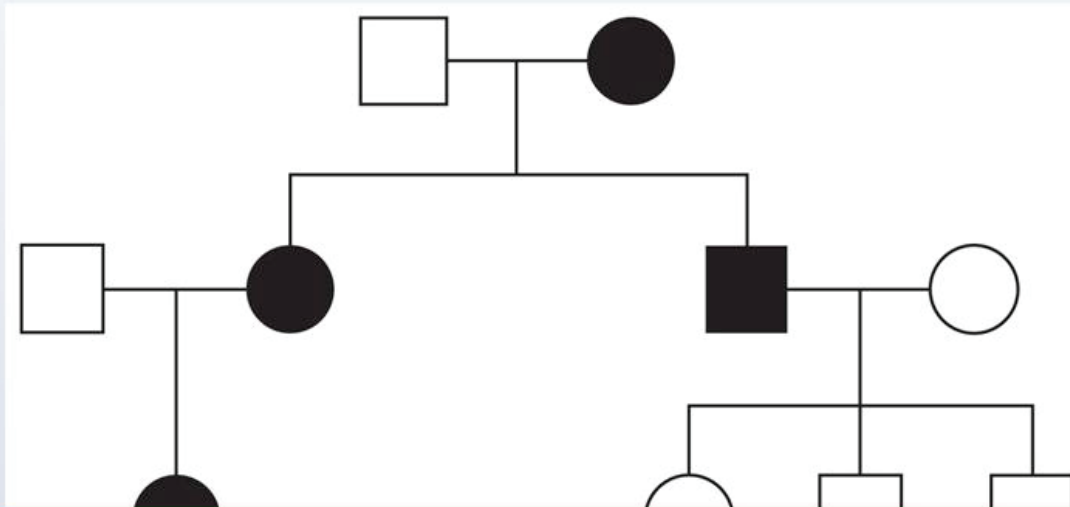


A 26-year-old woman is being evaluated for a possible inherited disorder. She has a 6-year history of generalized tonic-clonic seizures, and a year ago, she had partial loss of vision due to an occipital infarction. Her mother has chronic intermittent muscle weakness and lactic acidosis, and her maternal uncle has hemiplegia. Skeletal muscle biopsy of the patient shows ragged-appearing muscle fibers. After further evaluation, all the affected family members are found to suffer from the same inherited disease. Pedigree analysis is shown in the image below.



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12

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14

15

16

17

18

19

20

21

22

23

24

25

26

27

Item 1 of 40

Question Id: 1935

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display

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graph TD
    I1[Unshaded Male] --- I2[Shaded Female]
    I1 --- II1[Unshaded Male]
    I1 --- II2[Shaded Female]
    I2 --- II3[Shaded Male]
    I2 --- II4[Unshaded Female]
    II1 --- III1[Shaded Female]
    II3 --- III2[Unshaded Female]
    II3 --- III3[Unshaded Male]
    II3 --- III4[Unshaded Male]
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Zoom In

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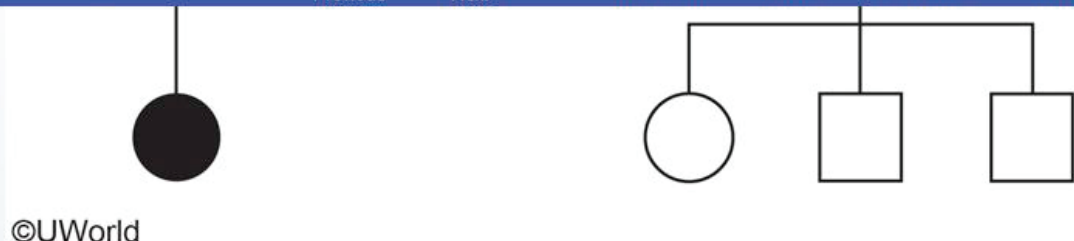
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Feedback

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Which of the following is the most likely explanation for the variability of clinical manifestations in the affected family members?

- ☐ A. Anticipation
- ☐ B. Heteroplasmy
- ☐ C. Incomplete penetrance
- ☐ D. Mosaicism
- ☐ E. Uniparental disomy

Submit





Which of the following is the most likely explanation for the variability of clinical manifestations in the affected family members?

- ☐ A. Anticipation (2%)
- ☒ B. Heteroplasmy (69%)
- ☐ C. Incomplete penetrance (12%)
- ☐ D. Mosaicism (9%)
- ☐ E. Uniparental disomy (5%)

Correct

69%
Answered correctly

01 min, 04 secs
Time Spent

02/23/2021
Last Updated

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Previous



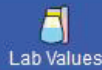
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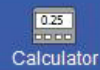
Tutorial



Lab Values



Notes



Calculator



Reverse Color



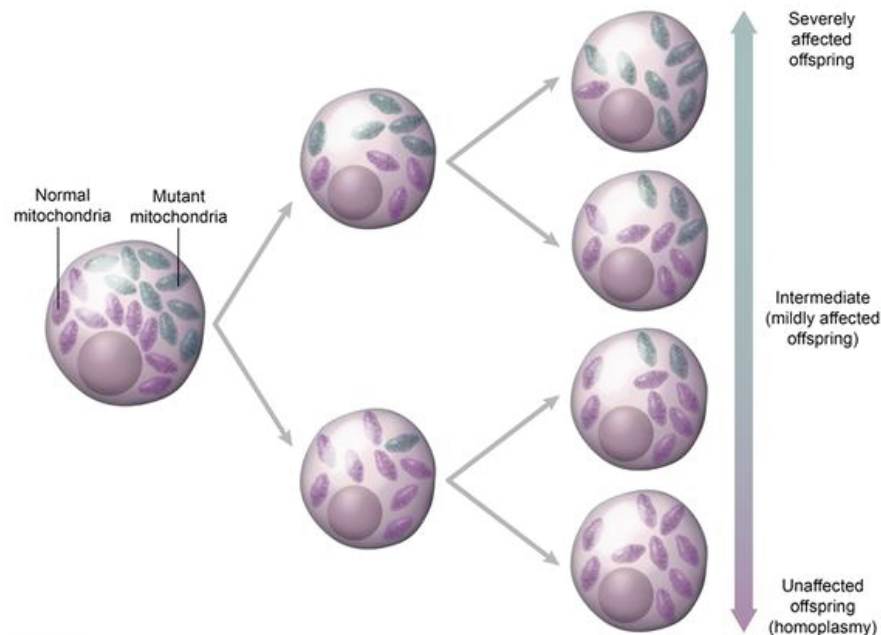
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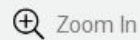
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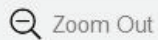
Heteroplasmy



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My Notebook

My Notebook



1



Feedback



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The neuromuscular lesions, ragged skeletal muscle fibers, and lactic acidosis in these family members suggest **mitochondrial encephalomyopathy**. Mitochondrial disorders follow a **maternal inheritance pattern** because an embryo's mitochondria are inherited from the ovum only.

Mitochondria are responsible for ATP production via oxidative phosphorylation, which is why mitochondrial defects tend to cause lactic acidosis and primarily affect tissues with the highest metabolic rates (eg, neural tissue, muscular tissue). Although many mitochondrial proteins are coded for in the nuclear genome, mitochondria also contain their own genome, which is vulnerable to mutations. Each cell has hundreds of mitochondria, and defects in their genome may occur in any number of the mitochondria within the cell.

Heteroplasmy describes the condition of having **different mitochondrial genomes** within a single cell.

The severity of mitochondrial diseases is often directly related to the proportion of abnormal to normal mitochondria within a patient's cells.

(Choice A) Anticipation refers to increased severity or earlier onset of an inherited disease in successive generations. It is commonly seen in autosomal and X-linked trinucleotide repeat disorders due to trinucleotide amplification during gametogenesis.

(Choice C) Penetrance is the probability that a person with a given genotype will express its associated phenotype. If all individuals with a given gene express its phenotype, that gene is said to have complete





(Choice C) Penetrance is the probability that a person with a given genotype will express its associated phenotype. If all individuals with a given gene express its phenotype, that gene is said to have complete penetrance.

(Choice D) Mosaicism refers to the presence of 2 or more cell lines, each with a unique nuclear genome, within the same individual. While patients with combined somatic and germline mosaicism can demonstrate disease traits and also pass the disease on to their offspring, mosaicism would not explain the pattern of female-only transmission.

(Choice E) Uniparental disomy occurs when both members of a chromosomal pair are inherited from one parent, which can cause problems due to genomic imprinting. For instance, although most often due to chromosomal deletions, uniparental disomy can also cause Prader-Willi and Angelman syndromes due to loss of expression of maternal/paternal imprinted components of a critical region of chromosome 15.

Educational objective:

The presence of lactic acidosis and ragged skeletal muscle fibers histologically suggests a mitochondrial myopathy. Variable clinical expressions in affected family members can occur due to heteroplasmy, which is the coexistence of distinct versions of mitochondrial genomes in an individual cell.

References





A 46-year-old man comes to the office due to right shoulder pain. The pain started 2 months ago after the patient began working at a new warehouse where he frequently moves heavy boxes. He has been taking over-the-counter analgesics and has continued to work. Past medical history is not significant. On physical examination, external rotation of the right shoulder against resistance is painful, but there is no weakness. MRI reveals near complete tear of the right infraspinatus muscle. The absence of weakness in this patient is best explained by compensatory hypertrophy of which of the following muscles?

- ☐ A. Latissimus dorsi
- ☐ B. Serratus anterior
- ☐ C. Subscapularis
- ☐ D. Supraspinatus
- ☐ E. Teres minor

Submit



A 46-year-old man comes to the office due to right **shoulder pain**. The pain started 2 months ago after the patient began working at a new warehouse where he frequently moves heavy boxes. He has been taking over-the-counter analgesics and has continued to work. Past medical history is not significant. On physical examination, **external rotation** of the right shoulder against resistance is painful, but there is no weakness. MRI reveals near complete tear of the right **infraspinatus muscle**. The absence of weakness in this patient is best explained by compensatory hypertrophy of which of the following muscles?

- ☐ A. Latissimus dorsi (6%)
- ☐ B. Serratus anterior (2%)
- ☐ C. Subscapularis (10%)
- ☐ D. Supraspinatus (12%)
- ☒ E. Teres minor (67%)

Correct



67%

Answered correctly



01 min, 38 secs

Time Spent



02/14/2021

Last Updated

Block Time Remaining: 00:02:43

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Rotator cuff muscles

| Muscle | Origin on scapula | Attachment on humerus | Function on arm | Innervation |
|---------------|--------------------|---|------------------------------------|---------------------------------|
| Supraspinatus | Supraspinous fossa | Superior aspect of greater tubercle | Abduction (primarily $<15^\circ$) | Suprascapular nerve |
| Infraspinatus | Infraspinous fossa | Posterolateral aspect of greater tubercle | External rotation | Suprascapular nerve |
| Teres minor | Lateral border | Posterolateral aspect of greater tubercle | Adduction & external rotation | Axillary nerve |
| Subscapularis | Subscapular fossa | Lesser tubercle | Adduction & internal rotation | Upper & lower subscapular nerve |

The **rotator cuff muscles** originate from the scapula and insert onto the proximal humerus; they stabilize the shoulder joint and move the arm at the shoulder. Overuse (eg, heavy lifting) can lead to rotator cuff injury, resulting in shoulder pain and possible weakness; the specific symptoms depend on which muscle is involved.

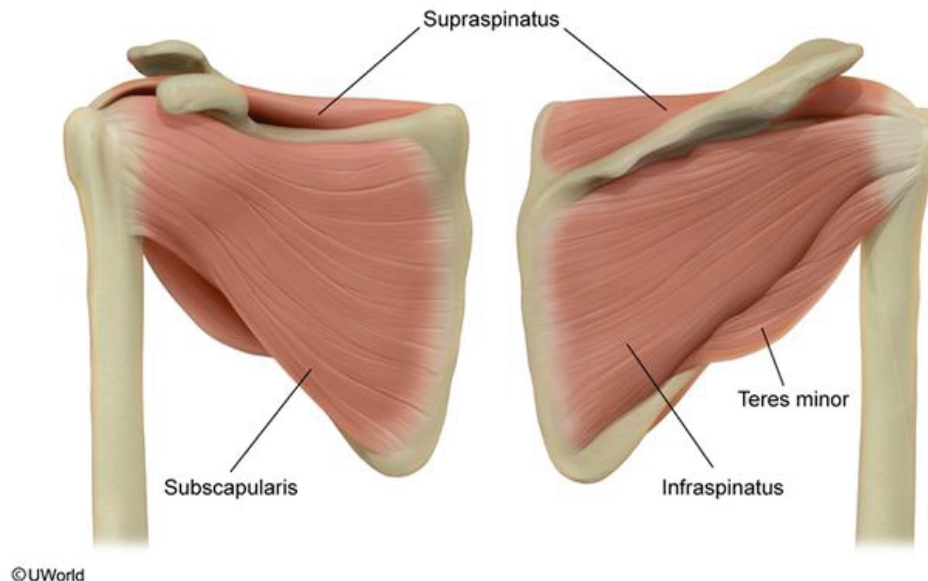


Exhibit Display

Rotator cuff muscles

Anterior view

Posterior view



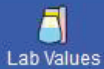
Zoom In

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fossa

internal rotation

subscapular nerve

The **rotator cuff muscles** originate from the scapula and insert onto the proximal humerus; they stabilize the shoulder joint and move the arm at the shoulder. Overuse (eg, heavy lifting) can lead to rotator cuff injury, resulting in shoulder pain and possible weakness; the specific symptoms depend on which muscle is involved.

Resistance added by the examiner when testing muscle function increases tendon loading, eliciting pain when tendon pathology is present. This patient has **pain** on resisted **external rotation**, suggesting pathology of the **infraspinatus or teres minor**, the two rotator cuff muscles responsible for this function.

The infraspinatus is the main external rotator when the arm is adducted (eg, by the side), whereas teres minor is the main external rotator when the arm is abducted. When the **infraspinatus tendon is torn**, there is often compensatory **hypertrophy of the teres minor**, thereby preserving the strength of external rotation.

(Choice A) **Latissimus dorsi** is a broad muscle in the mid- and low back. It originates from the spinous processes of T7 to L5, iliac crest, thoracolumbar fascia, inferior angle of the scapula, and the lower 3 or 4 ribs. It inserts onto the bicipital groove of the humerus and adducts, extends, and internally (not externally) rotates the arm.



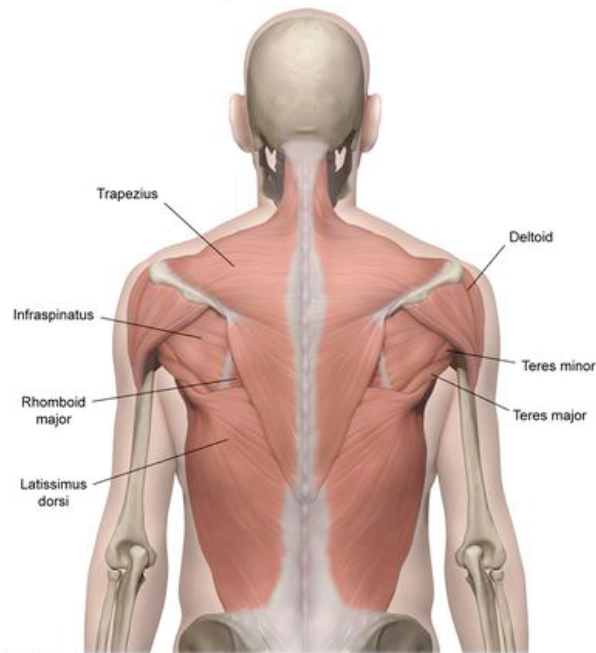
fossa

internal rotation

subscapular nerve

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Superficial back muscles



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rotates the arm.

(Choice B) [Serratus anterior](#) is a fan-shaped muscle in the lateral thorax. It originates from the first 8 or 9 ribs and inserts onto various sections of the scapula. It is responsible for anterolateral and rotational movements of the scapula. When the long thoracic nerve is damaged, the muscle becomes paralyzed, resulting in [winged scapula](#).

(Choice C) Subscapularis originates from the subscapular fossa of the scapula and inserts onto the lesser tubercle of the humerus. It adducts and internally (not externally) rotates the arm.

(Choice D) Supraspinatus originates from the supraspinatus fossa of the scapula and inserts onto the superior aspect of the greater tubercle of the humerus. It abducts the arm.

Educational objective:

The rotator cuff muscles attach to the proximal humerus and move the arm at the shoulder. Infraspinatus and teres minor are primarily responsible for external rotation. When one is torn, the other hypertrophies to compensate, resulting in preserved strength in external rotation.

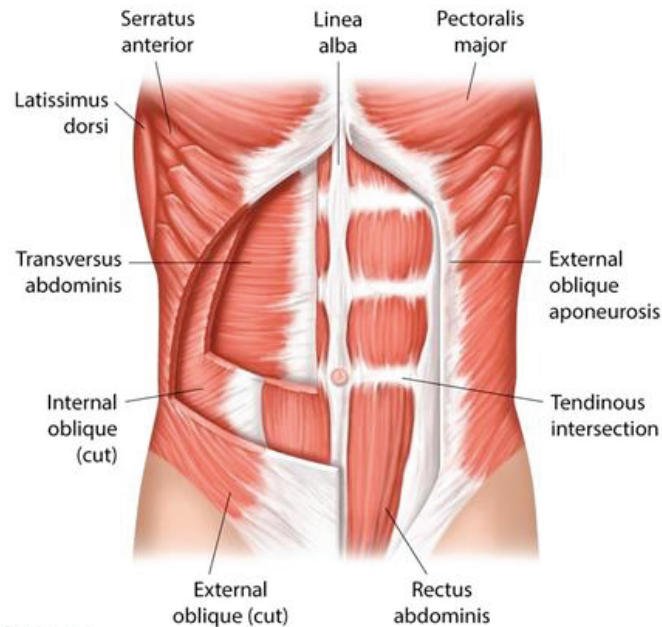
References

- [Acute shoulder injuries in adults](#).

rotates the arm.

Exhibit Display

Abdominal wall musculature



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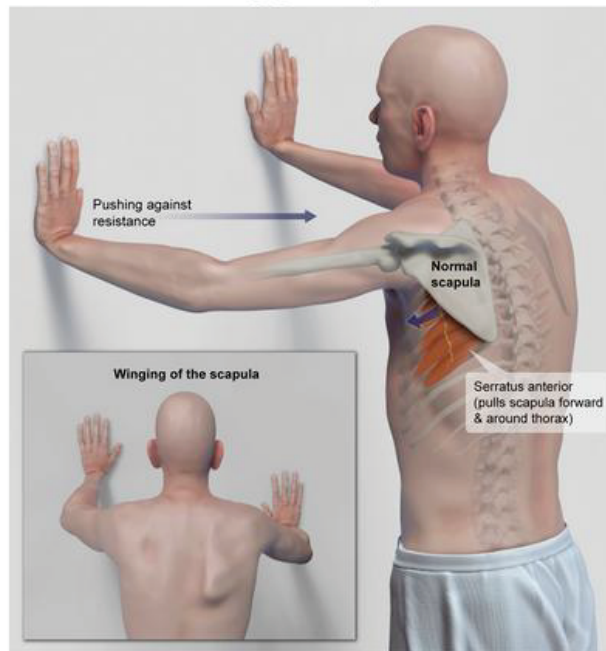
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rotates the arm.

Exhibit Display

Winging of the scapula



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A 74-year-old woman comes to the emergency department due to left hip pain and inability to walk after a fall. She is being treated by her primary care provider for various medical conditions including hypertension, congestive heart failure, chronic atrial fibrillation, type 2 diabetes mellitus, trigeminal neuralgia, depression, and gastroesophageal reflux disease. On examination, the left leg is shorter than the right and externally rotated. She is not able to move the left hip. An imaging study confirms acute femoral neck fracture. Her bone density, measured by quantitative x-ray densitometry, is consistent with osteoporosis. Which of the following drugs, had it been used as part of the medical regimen, would have had a beneficial effect on calcium homeostasis and reduced this patient's fracture risk?

- ☐ A. Carbamazepine
- ☐ B. Diltiazem
- ☐ C. Escitalopram
- ☐ D. Furosemide
- ☐ E. Hydrochlorothiazide
- ☐ F. Lansoprazole





neuralgia, depression, and gastroesophageal reflux disease. On examination, the left leg is shorter than the right and externally rotated. She is not able to move the left hip. An imaging study confirms acute femoral neck fracture. Her bone density, measured by quantitative x-ray densitometry, is consistent with osteoporosis. Which of the following drugs, had it been used as part of the medical regimen, would have had a beneficial effect on calcium homeostasis and reduced this patient's fracture risk?

- ☐ A. Carbamazepine
- ☐ B. Diltiazem
- ☐ C. Escitalopram
- ☐ D. Furosemide
- ☐ E. Hydrochlorothiazide
- ☐ F. Lansoprazole
- ☐ G. Metformin
- ☐ H. Spironolactone





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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femoral neck fracture. Her bone density, measured by quantitative x-ray densitometry, is consistent with osteoporosis. Which of the following drugs, had it been used as part of the medical regimen, would have had a beneficial effect on calcium homeostasis and reduced this patient's fracture risk?

- ☐ A. Carbamazepine (0%)
- ☐ B. Diltiazem (2%)
- ☐ C. Escitalopram (2%)
- ☐ D. Furosemide (4%)
- ☒ E. Hydrochlorothiazide (81%)
- ☐ F. Lansoprazole (2%)
- ☐ G. Metformin (1%)
- ☐ H. Spironolactone (5%)

Correct

81%



01 min, 36 secs



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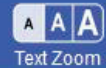
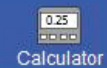
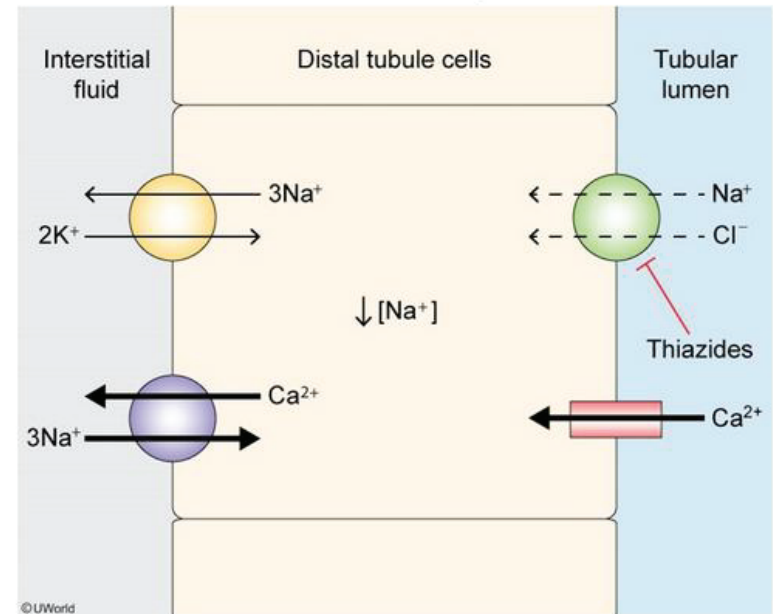


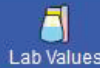
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Effect of thiazide diuretics on distal tubular calcium reabsorption



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Thiazide diuretics (eg, hydrochlorothiazide, chlorthalidone) are indicated for treatment of patients with hypertension, including those who also have diabetes mellitus. Although thiazides can cause a small increase in blood glucose, this effect is often not clinically significant and substantially outweighed by their blood pressure-lowering benefits.

Thiazides inhibit the **Na-Cl cotransporter** in the distal convoluted tubule, leading to decreased sodium reabsorption. Thiazides also cause peripheral vasodilation, resulting in reduced peripheral vascular resistance. In addition, thiazide diuretics increase **calcium reabsorption** in the distal tubule. Studies have shown that use of thiazides is associated with higher bone mineral density and reduced fracture risk, and many experts recommend them for treatment of hypertension in patients who are at risk for osteoporosis. Increased calcium reabsorption also causes hypocalciuria, which may prevent recurrent renal stones in some patients.

(Choice A) Several antiepileptic drugs (eg, phenytoin, carbamazepine, phenobarbital) are associated with decreased bone mineral density and increased risk of osteoporosis.

(Choice B) Diltiazem is a calcium channel blocker that is indicated for treatment of hypertension. It is also used for rate control in patients with atrial fibrillation. It has no significant effect on serum calcium levels, bone density, or fracture risk.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) Diltiazem is a calcium channel blocker that is indicated for treatment of hypertension. It is also used for rate control in patients with atrial fibrillation. It has no significant effect on serum calcium levels, bone density, or fracture risk.

(Choice C) Escitalopram is a selective serotonin reuptake inhibitor (SSRI) indicated for treatment of depression and generalized anxiety disorder. SSRIs are associated with a small decrease in bone density; their effect on fracture risk has not been well studied.

(Choice D) Furosemide is a loop diuretic used to treat congestive heart failure (CHF). It causes an increase in urinary calcium loss that may worsen osteoporosis.

(Choice F) Lansoprazole is a proton pump inhibitor (PPI) used to treat gastroesophageal reflux and peptic ulcer. PPIs inhibit the enzyme H-K-ATPase on gastric parietal cells and reduce gastric acid secretion. PPIs also decrease calcium and magnesium absorption, and long-term use is associated with an increased risk of osteoporosis.

(Choice G) Metformin suppresses hepatic gluconeogenesis and increases insulin sensitivity and peripheral glucose uptake. It has no significant effect on osteoporosis risk.

(Choice H) Spironolactone is an aldosterone inhibitor used to treat CHF. Spironolactone can cause hyperkalemia, but it does not have a significant effect on calcium homeostasis.



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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(Choice D) Furosemide is a loop diuretic used to treat congestive heart failure (CHF). It causes an increase in urinary calcium loss that may worsen osteoporosis.

(Choice F) Lansoprazole is a proton pump inhibitor (PPI) used to treat gastroesophageal reflux and peptic ulcer. PPIs inhibit the enzyme H-K-ATPase on gastric parietal cells and reduce gastric acid secretion. PPIs also decrease calcium and magnesium absorption, and long-term use is associated with an increased risk of osteoporosis.

(Choice G) Metformin suppresses hepatic gluconeogenesis and increases insulin sensitivity and peripheral glucose uptake. It has no significant effect on osteoporosis risk.

(Choice H) Spironolactone is an aldosterone inhibitor used to treat CHF. Spironolactone can cause hyperkalemia, but it does not have a significant effect on calcium homeostasis.

Educational objective:

Thiazide diuretics increase calcium absorption in the distal convoluted tubules within the nephron.

Thiazides are associated with increased bone mineral density and are recommended for treatment of hypertension in patients at risk for osteoporosis. Loop diuretics increase urinary calcium loss.

References



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A 68-year-old woman with end-stage renal disease receiving intermittent hemodialysis comes to the office due to back pain. She says that she may have "pulled a muscle" while getting out of her car a week ago; since then she has had progressively worsening back pain. She has no leg numbness or weakness but reports malaise and fatigue. The patient also has hypertension and type 2 diabetes mellitus and was treated several weeks ago for staphylococcal bacteremia associated with the dialysis catheter. Her temperature is 38 C (100.4 F). On examination, she has tenderness over the upper lumbar vertebrae without overlying skin changes. The straight leg raise test is negative. Which of the following is the best next step in management of this patient?

- ☐ A. Analgesics and close follow-up
- ☐ B. CT myelogram
- ☐ C. Lumbar puncture
- ☐ D. MRI of the spine
- ☐ E. Serum protein electrophoresis





due to **back pain**. She says that she may have "pulled a muscle" while getting out of her car a week ago; since then she has had progressively worsening back pain. She has no leg numbness or weakness but reports **malaise** and fatigue. The patient also has hypertension and type 2 diabetes mellitus and was treated several weeks ago for **staphylococcal bacteremia** associated with the dialysis catheter. Her temperature is 38 C (100.4 F). On examination, she has tenderness over the upper lumbar vertebrae without overlying skin changes. The straight leg raise test is negative. Which of the following is the best next step in management of this patient?

- ☐ A. Analgesics and close follow-up (7%)
- ☐ B. CT myelogram (10%)
- ☐ C. Lumbar puncture (13%)
- ☒ D. MRI of the spine (51%)
- ☐ E. Serum protein electrophoresis (15%)

Correct

51%
Answered correctly01 min, 03 secs
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Feedback



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Although this patient believes her back pain may be due to a muscle sprain, her presentation (localized bony back pain, low-grade fever, recent staphylococcal bacteremia) suggests **vertebral osteomyelitis**. Bacteria can access the spine by hematogenous spread from a distant infection (eg, skin or soft tissue, intravenous catheter), direct invasion from trauma or local spinal procedures (eg, lumbar puncture, spinal surgery), or direct spread from adjacent soft tissue infection. **Hematogenous** spread is most common as the adult vertebral bone has a very rich and vascular marrow. Increasing age can cause the nutrient arteries to develop a "corkscrew" anatomy, which allows bacteria to more easily penetrate the marrow cavity and cause local infection.

Bacteremia due to intravascular devices (eg, hemodialysis catheters) increases risk of health care-related vertebral osteomyelitis. Offending organisms include ***Staphylococcus*** (most common is *S aureus* or coagulase-negative staphylococci) and various gram-negative organisms (eg, *Pseudomonas*). Vertebral osteomyelitis should be suspected in patients with new or worsening back pain, fever, and recent endocarditis or bacteremia (especially *S aureus*). It should also be suspected if there are new neurologic findings and fever, with or without back pain. Initial evaluation includes **blood cultures** and **MRI** of the spine, which is the most sensitive imaging method for diagnosing vertebral osteomyelitis.

(Choice A) Analgesics and close follow-up are recommended for musculoskeletal causes of low back



spine, which is the most sensitive imaging method for diagnosing vertebral osteomyelitis.

(Choice A) Analgesics and close follow-up are recommended for musculoskeletal causes of low back pain, but this patient's clinical findings (fever, localized bony tenderness, recent bacteremia) are concerning for more serious etiologies and require further evaluation.

(Choice B) CT myelogram, which can diagnose spinal stenosis or other vertebral pathology (including osteomyelitis), is performed by injecting contrast into the lumbar spine prior to CT imaging. However, it is more invasive than MRI and usually reserved for patients who cannot undergo MRI (eg, those with pacemaker, metallic implants).

(Choice C) Lumbar puncture is typically used for diagnosing meningitis and has a low yield for diagnosing vertebral osteomyelitis. CT-guided bone biopsy is usually preferred for isolating the organism after imaging confirms the diagnosis of vertebral osteomyelitis.

(Choice E) Serum protein electrophoresis is typically done to evaluate for monoclonal gammopathies (eg, multiple myeloma). Although multiple myeloma can present with back pain, this patient's fever and recent bacteremia make vertebral osteomyelitis more likely.

Educational objective:



pacemaker, metallic implants).

(Choice C) Lumbar puncture is typically used for diagnosing meningitis and has a low yield for diagnosing vertebral osteomyelitis. CT-guided bone biopsy is usually preferred for isolating the organism after imaging confirms the diagnosis of vertebral osteomyelitis.

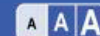
(Choice E) Serum protein electrophoresis is typically done to evaluate for monoclonal gammopathies (eg, multiple myeloma). Although multiple myeloma can present with back pain, this patient's fever and recent bacteremia make vertebral osteomyelitis more likely.

Educational objective:

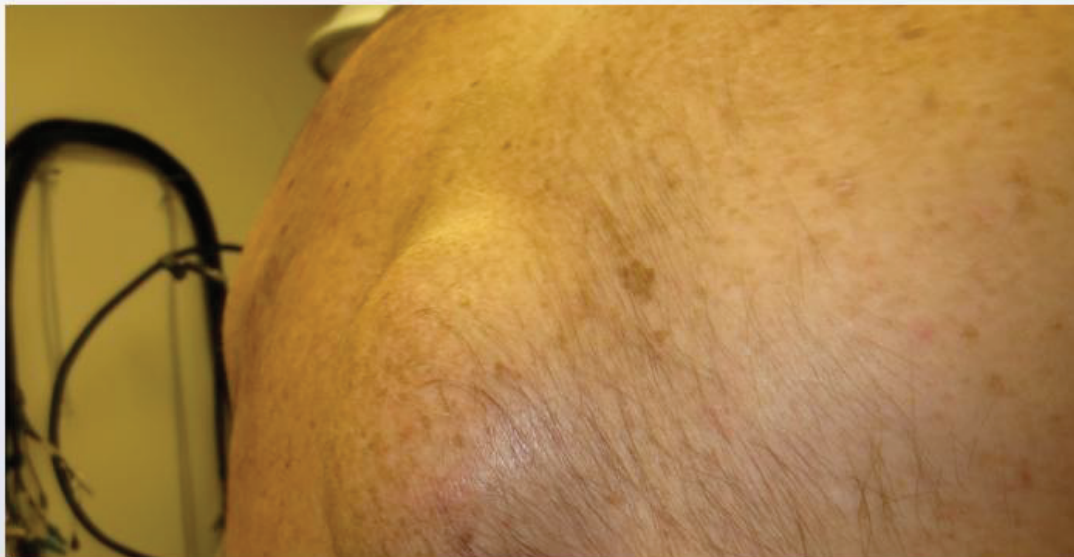
Vertebral osteomyelitis should be suspected in patients with new or worsening back pain, fever, and recent endocarditis or bacteremia (especially *Staphylococcus aureus*). It should also be suspected if there are new neurologic findings and fever with or without back pain. MRI of the spine is preferred for diagnosis.

References

- 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults.
- Health care associated hematogenous pyogenic vertebral osteomyelitis: a severe and potentially preventable infectious disease



A 50-year-old man comes to the office for evaluation of a mass on his back. He has had the mass for several years, and it has increased only slightly in size during that time. The patient has 2 other similar lesions, one on his arm and the other on his leg. The lesions are painless, and he has no other symptoms. Vitals signs are normal. Examination shows multiple subcutaneous, soft, freely mobile, and nontender masses. The lesion on his back is shown in the image.





Item 5 of 40

Question Id: 15665



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Zoom Out

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Block Time Remaining: 00:05:27

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End Block



Histologic examination of the mass is most likely to show which of the following findings?

- ☐ A. Mature adipocytes arranged in lobules and separated by fibrous septa
- ☐ B. Pleomorphic malignant cells producing new woven bone
- ☐ C. Septal panniculitis with a mixed cellular infiltrate of lymphocytes and histiocytes
- ☐ D. Sheets of polygonal cells with prominent intercellular bridges and keratinization
- ☐ E. Spindle cells with wavy nuclei embedded in collagen stroma

Submit





Histologic examination of the mass is most likely to show which of the following findings?

- ☒ A. Mature adipocytes arranged in lobules and separated by fibrous septa (91%)
- ☐ B. ~~Pleomorphic malignant cells producing new woven bone (0%)~~
- ☐ C. Septal panniculitis with a mixed cellular infiltrate of lymphocytes and histiocytes (2%)
- ☐ D. ~~Sheets of polygonal cells with prominent intercellular bridges and keratinization (1%)~~
- ☐ E. ~~Spindle cells with wavy nuclei embedded in collagen stroma (4%)~~

Correct

91%
Answered correctly



01 min, 22 secs
Time Spent



12/15/2020
Last Updated

Block Time Remaining: 00:06:44

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Suspend



End Block

This patient has a **soft, mobile, subcutaneous mass** consistent with a lipoma. **Lipomas** are very common, **benign** tumors that arise from the subcutaneous fat. They typically occur in middle-aged adults and are generally stable or **enlarge slowly** over time. The overlying **epidermis is normal**.

The diagnosis of lipoma is usually easy to make on clinical examination. However, if necessary, **excisional biopsy** can be performed and shows well-differentiated, **mature adipocytes** with an intact fibrous capsule. Because lipomas are generally harmless, most can be left in place, although excision can be considered for cosmetic reasons or patient discomfort.

(Choice B) **Osteosarcoma** is usually seen in children and young adults; it is uncommon in older adults, in which it is often associated with Paget disease of bone. It presents with local pain and swelling; the mass, if palpable, is nonmobile. Histopathology shows pleomorphic malignant cells with hyperchromatic nuclei forming neoplastic osteoid or bone.

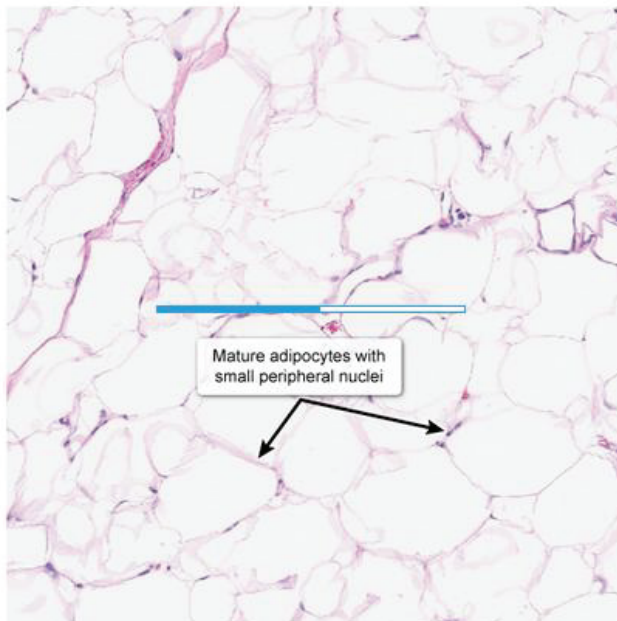
(Choice C) **Erythema nodosum** presents acutely as tender, subcutaneous nodules in the lower extremities. It occurs in association with a variety of infectious (eg, herpes simplex) and inflammatory (eg, sarcoidosis) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with edema, fibrinous exudate, and a variable cellular infiltrate (neutrophils, lymphocytes, histiocytes).

(Choice D) **Cutaneous squamous cell carcinoma** typically forms an enlarging epidermal nodule in sun

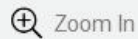


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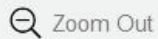
Lipoma



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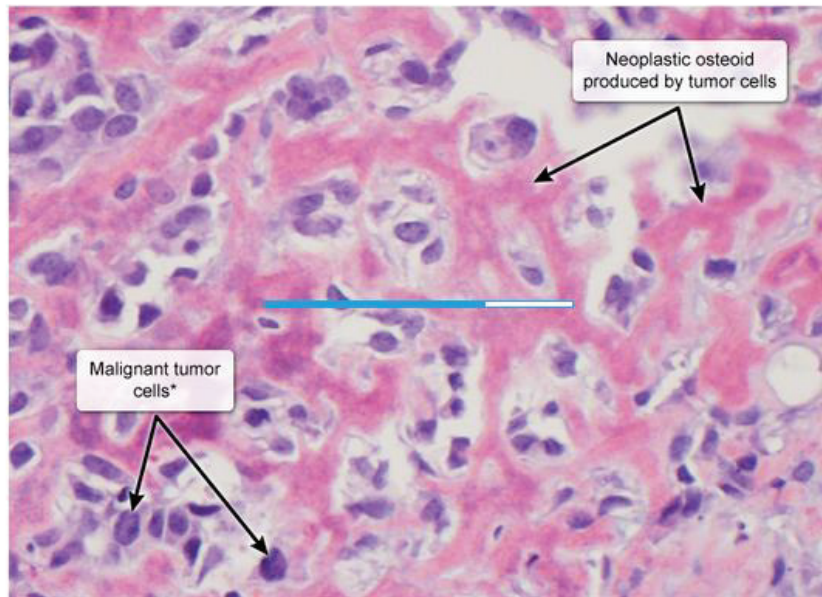
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Osteosarcoma



*Pleomorphic cells with hyperchromatic nuclei

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Item 5 of 40

Question Id: 15665



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



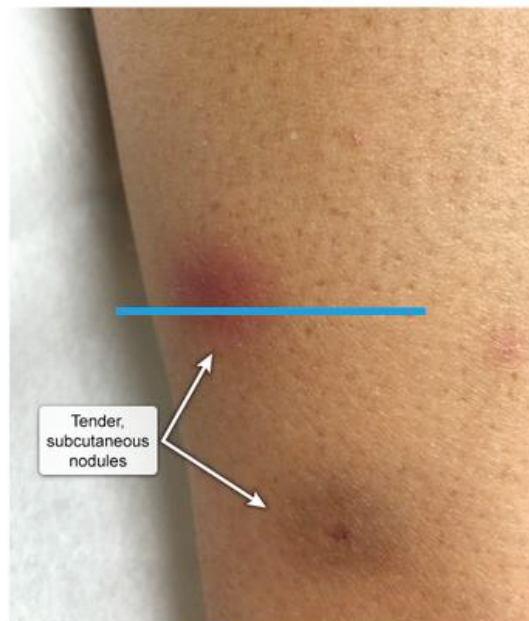
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Erythema nodosum



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Feedback



Suspend



End Block



sarcoidosis) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with edema, fibrinous exudate, and a variable cellular infiltrate (neutrophils, lymphocytes, histiocytes).

(Choice D) [Cutaneous squamous cell carcinoma](#) typically forms an enlarging epidermal nodule in sun-exposed areas. The lesions often develop a thickened, rough surface or ulcerate with crusting and bleeding. Pathologic findings include sheets of eosinophilic squamous cells with [keratin pearls](#) and [intercellular bridges](#).

(Choice E) Cutaneous [neurofibromas](#) usually manifest during early adolescence as raised, fleshy tumors (<2 cm) that often increase in size and number with age. They are composed primarily of [Schwann cells](#) (spindle-shaped cells with wavy or serpentine nuclei), fibroblasts, and perineural cells.

Educational objective:

Lipomas are common, benign tumors that arise from the subcutaneous fat and present as soft, mobile masses that are stable or enlarge slowly over time. The diagnosis is usually made clinically, but histopathology shows well-differentiated, mature adipocytes with a fibrous capsule.

References

- [Lipomas, pathology.](#)





carcinoides) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with

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Cutaneous squamous cell carcinoma



Rough, ulcerative
lesion

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Zoom In



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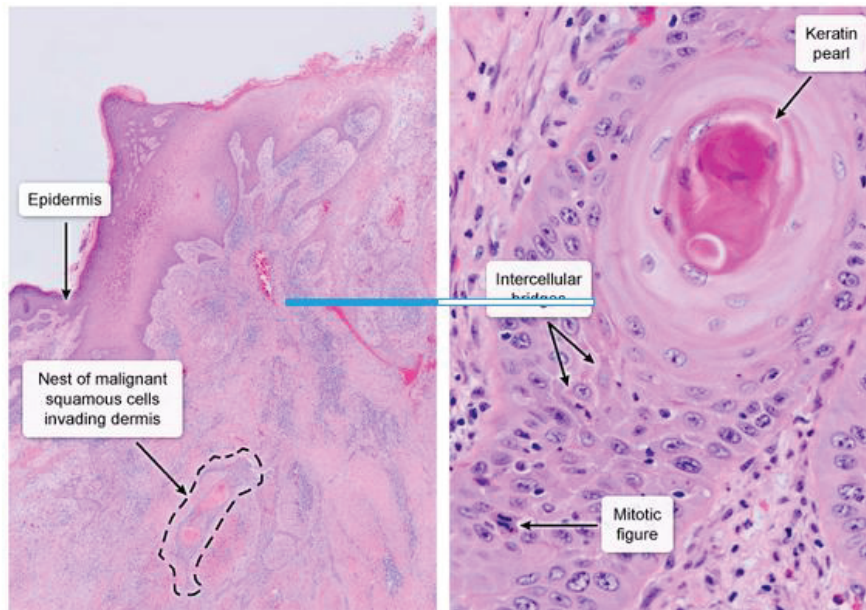




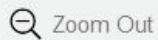
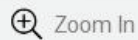
carcinoidosis) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with

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Cutaneous squamous cell carcinoma



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carcinoidosis) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with

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Neurofibromatosis



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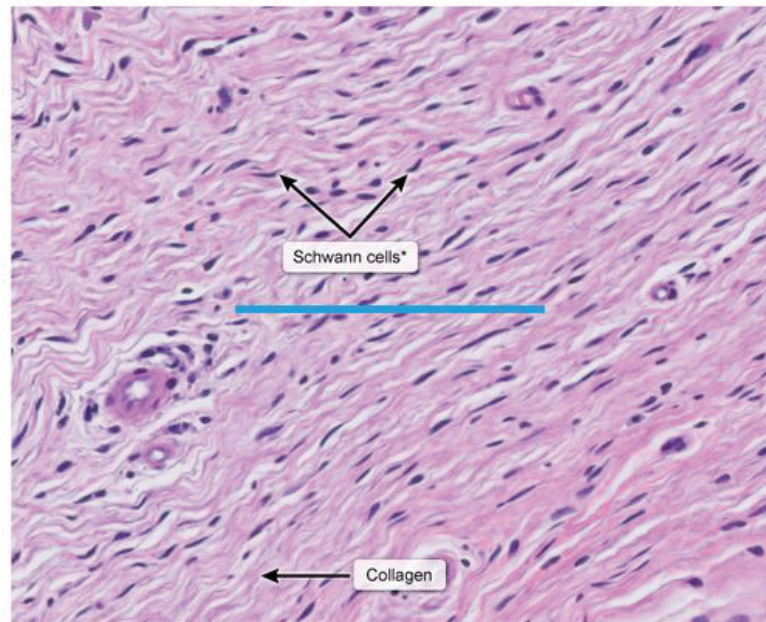




carcinoidosis) conditions. Histopathology shows inflammation in the subcutaneous fat (panniculitis) with

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Neurofibroma



*Spindle-shaped cells with wavy nuclei

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Zoom In



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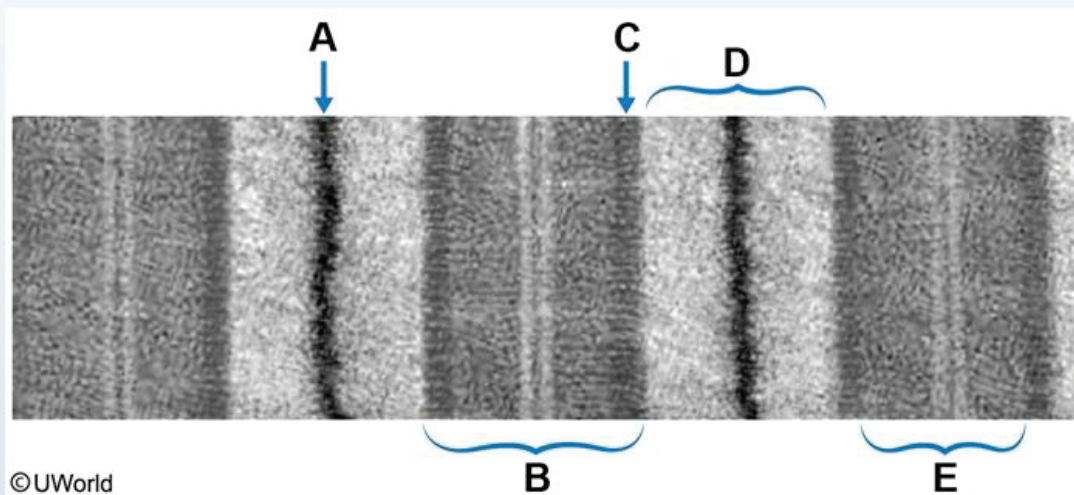


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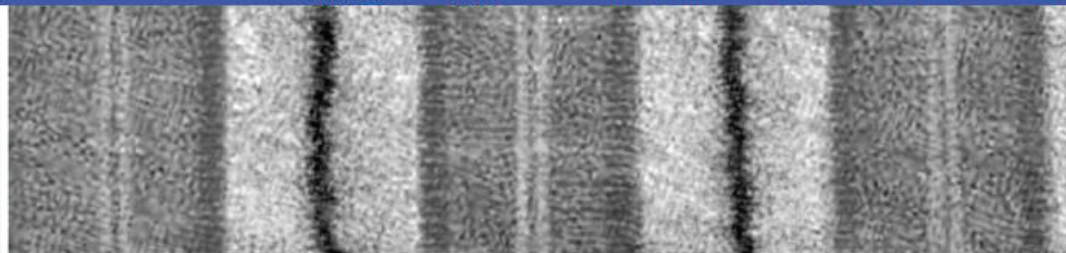
An 8-year-old boy is evaluated in the office due to difficulty walking. The patient has problems running, jumping, and walking up steps. There is no history of neurological disorders in the family. Physical examination reveals weakness of lower extremity muscles bilaterally. Electron microscopy of a biopsy sample taken from calf muscle is shown below.



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Which of the following labeled regions contains only thick filaments and no thin filaments?





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B

E

Which of the following labeled regions contains only thick filaments and no thin filaments?

- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit

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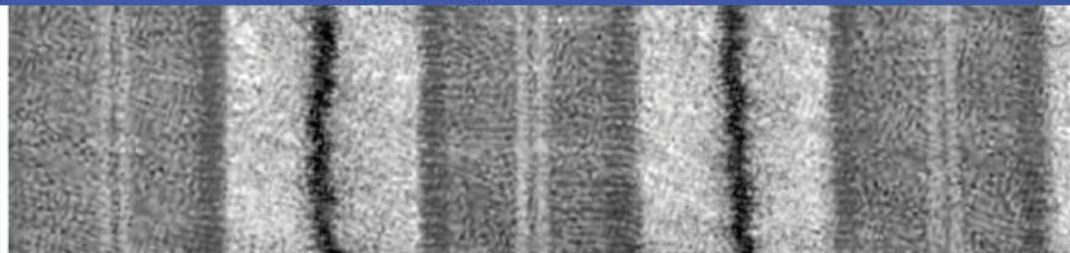
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B**E**

Which of the following labeled regions contains only thick filaments and no thin filaments?

- ☐ A.A (10%)
- ☐ B.B (10%)
- ☐ C.C (8%)
- ☐ D.D (10%)
- ☒ E.E (61%)



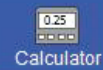
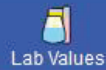
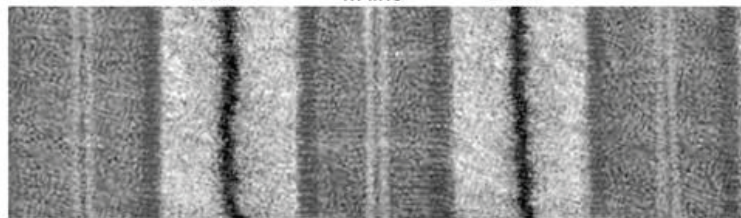


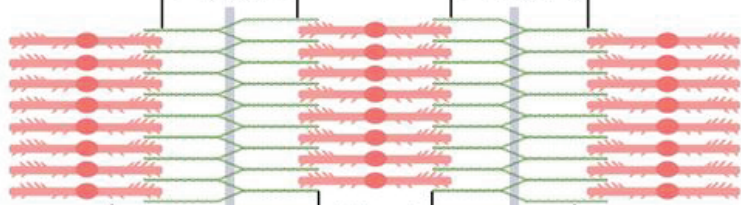
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Sarcomere
(Z to Z)

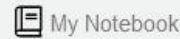
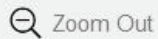
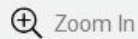
Z line M line Z line



I band A band I band

Thick myofilament
(myosin)Thin myofilament
(actin)

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(myosin)

(actin)

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The **H band** is the region of the sarcomere containing only **thick (myosin) filaments**. On electron microscopy, the H band is a portion of the A band that **straddles the M line**. The A band corresponds to the thick filaments in the sarcomere and includes portions overlapped by thin (actin) filaments (**Choice B**). During muscle contraction, the thin filaments slide over the thick filaments toward the M line, reducing the length of the H band. The A band always remains the same length.

(Choice A) The Z line is typically distinctly darker than the remainder of the sarcomere. Thin filaments, which are composed of actin, tropomyosin, and troponin, anchor at the Z line.

(Choice C) The segment of the sarcomere between the H and I bands is where thick and thin filaments overlap.

(Choice D) The I band contains the Z line and only those sections of the thin filaments that do not overlap with thick filaments. During muscle contraction, both the I band and H band decrease in length.

Educational objective:

The H band is the region of the sarcomere that contains only thick (myosin) filaments. The H band is the part of the A band (which is on either side of the M line) where thick filaments have no overlapping thin (actin) filaments.





A 65-year-old woman is concerned about her risk of fracture as her mother was recently hospitalized for osteoporotic hip fracture. The patient walks her dog for a mile on most days and has no problems with balance or falling. She has a history of hypertension, hyperlipidemia, coronary artery disease, seizure disorder, and gastroesophageal reflux disease. The patient underwent menopause at age 52. She has smoked a pack of cigarettes daily for 24 years but does not drink alcohol. Weight is 56 kg (123.5 lb). Long-term use of which of the following medications may increase this patient's risk of osteoporosis and hip fracture?

- ☐ A. Atorvastatin
- ☐ B. Chlorthalidone
- ☐ C. Levetiracetam
- ☐ D. Metoprolol
- ☐ E. Nitroglycerin
- ☐ F. Omeprazole





osteoporotic hip fracture. The patient walks her dog for a mile on most days and has no problems with balance or falling. She has a history of hypertension, hyperlipidemia, coronary artery disease, seizure disorder, and gastroesophageal reflux disease. The patient underwent menopause at age 52. She has smoked a pack of cigarettes daily for 24 years but does not drink alcohol. Weight is 56 kg (123.5 lb). Long-term use of which of the following medications may increase this patient's risk of osteoporosis and hip fracture?

- ☐ A. Atorvastatin (5%)
- ☐ B. Chlorthalidone (15%)
- ☐ C. Levetiracetam (11%)
- ☐ D. Metoprolol (1%)
- ☐ E. Nitroglycerin (0%)
- ☒ F. Omeprazole (65%)

Correct

65%



55 secs



03/03/2021

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End Block



Medications associated with osteoporotic fractures

| Medication | Possible mechanism |
|---|---------------------------|
| Anticonvulsants that induce cytochrome P450 (phenobarbital, phenytoin, carbamazepine) | ↑ Vitamin D catabolism |
| Aromatase inhibitors | ↓ Estrogen |
| Medroxyprogesterone | |
| GnRH agonists | ↓ Testosterone & estrogen |
| Proton pump inhibitors | ↓ Calcium absorption |
| Glucocorticoids | ↓ Bone formation |

Insoluble calcium (eg, calcium carbonate) requires an acidic environment for proper absorption. Strong acid-suppressing medications, such as **proton pump inhibitors** (eg, omeprazole), may **decrease absorption of dietary calcium** in the gastrointestinal tract. Long-term use of these medications is associated with an increased risk of **osteoporotic fractures**. The risk is greatest in older adults in whom





Insoluble calcium (eg, calcium carbonate) requires an acidic environment for proper absorption. Strong acid-suppressing medications, such as **proton pump inhibitors** (eg, omeprazole), may **decrease absorption of dietary calcium** in the gastrointestinal tract. Long-term use of these medications is associated with an increased risk of **osteoporotic fractures**. The risk is greatest in older adults in whom calcium absorption is already reduced and in those with other risk factors for osteoporosis (eg, low body weight, smoking).

Medications that reduce bone formation (eg, glucocorticoids) can also increase the risk of osteoporosis. Because estrogen plays an important role in bone density, medications that decrease estrogen production (eg, aromatase inhibitors, GnRH agonists) can increase osteoporosis risk. In addition, anticonvulsants that induce the cytochrome P450 system in the liver (eg, phenytoin, carbamazepine) can increase catabolism of vitamin D and lead to lower bone density. Levetiracetam does not induce the P450 enzyme system and has not been shown to negatively affect bone mineral density in adults (**Choice C**).

(**Choice A**) Statins (eg, atorvastatin) do not increase the risk of osteoporosis, and some studies have noted increased bone density in patients taking these medications.

(**Choice B**) Thiazide diuretics (eg, chlorthalidone, hydrochlorothiazide) increase reabsorption of calcium in the distal renal tubule and are associated with a small decrease in the risk of osteoporosis.





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Previous

Next

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Tutorial

Lab Values

Notes

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(Choice A) Statins (eg, atorvastatin) do not increase the risk of osteoporosis, and some studies have noted increased bone density in patients taking these medications.

(Choice B) Thiazide diuretics (eg, chlorthalidone, hydrochlorothiazide) increase reabsorption of calcium in the distal renal tubule and are associated with a small decrease in the risk of osteoporosis.

(Choice D) Beta blockers (eg, metoprolol) may slightly decrease the risk of osteoporosis, possibly due to increased formation and decreased resorption of bone.

(Choice E) Nitrates (eg, nitroglycerin) have been associated in some studies with increased bone density, possibly due to decreased bone turnover.

Educational objective:

Long-term acid suppression with proton pump inhibitors may be associated with an increased risk of osteoporotic fractures, possibly due to decreased calcium absorption. Other medications associated with an increased risk of osteoporosis include glucocorticoids, aromatase inhibitors, and anticonvulsants that induce cytochrome P450.

References

- [Update on medications with adverse skeletal effects.](#)



1



Feedback



Suspend



End Block



A 2-year-old boy is evaluated for recurrent infections. He was born at term after a normal pregnancy. His mother states, "He is always sick with something and is constantly on antibiotics." The patient's past medical records indicate multiple episodes of otitis media, skin infections, and pneumonia. Incision and drainage of his skin infections revealed *Staphylococcus aureus* on bacterial culture but no purulence. His infections usually resolve with prolonged antibiotic courses. Laboratory testing reveals absent CD18 antigens on the surface of leukocytes. The patient is at greatest risk for which of the following?

- ☐ A. Infection following live-virus vaccines
- ☐ B. Infection with *Neisseria*
- ☐ C. Persistent leukocytosis
- ☐ D. Small or absent lymph nodes
- ☐ E. Thrombocytopenia and eczema

Submit



A 2-year-old boy is evaluated for recurrent infections. He was born at term after a normal pregnancy. His mother states, "He is always sick with something and is constantly on antibiotics." The patient's past medical records indicate multiple episodes of otitis media, skin infections, and pneumonia. Incision and drainage of his skin infections revealed *Staphylococcus aureus* on bacterial culture but no purulence. His infections usually resolve with prolonged antibiotic courses. Laboratory testing reveals absent CD18 antigens on the surface of leukocytes. The patient is at greatest risk for which of the following?

- ☐ A. Infection following live-virus vaccines (11%)
- ☐ B. Infection with *Neisseria* (18%)
- ☒ C. Persistent leukocytosis (51%)
- ☐ D. Small or absent lymph nodes (10%)
- ☐ E. Thrombocytopenia and eczema (8%)

Correct



51%

Answered correctly



01 min, 44 secs

Time Spent



03/12/2021

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Explanation

Leukocyte adhesion deficiency

| | |
|----------------------------|--|
| Pathophysiology | <ul style="list-style-type: none">• Defect in CD18-containing integrins• Impaired leukocyte adhesion & endothelial transmigration |
| Clinical features | <ul style="list-style-type: none">• Skin & mucosal infections (eg, cellulitis, periodontitis) without pus formation• Impaired wound healing• Delayed umbilical cord separation (age >3 weeks) |
| Laboratory findings | <ul style="list-style-type: none">• Leukocytosis & neutrophilia |

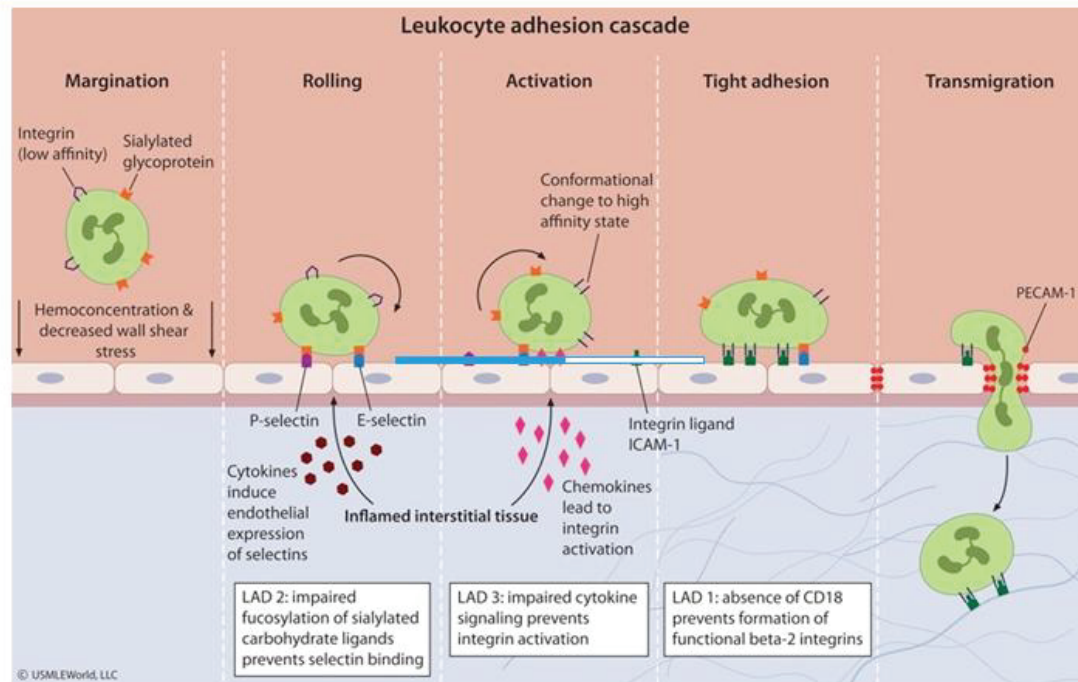
This patient's recurring skin and mucosal infections as well as absence of purulence are highly suggestive of **leukocyte adhesion deficiency** (LAD). LAD is an autosomal recessive disorder characterized by **absence of CD18** antigens, which are necessary for the formation of integrins. Integrins are essential for leukocyte **adhesion** to endothelial surfaces and migration to peripheral tissues in response to infection or inflammation.

The failure of leukocyte chemotaxis results in LAD findings, which include recurrent skin and mucosal





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The failure of leukocyte chemotaxis results in LAD findings, which include recurrent skin and mucosal infections (often due to *Staphylococcus aureus* or gram-negative rods) and periodontal disease. LAD-related infections are notable for **lack of purulence** due to absence of leukocytes in peripheral tissues. Wound healing is also impaired, including **late separation** (>21 days) of the umbilical cord. **Persistent leukocytosis** is a common finding due to leukocytes not being able to migrate out of the blood vessels.

(Choice A) Deficiencies of T cell-mediated immunity (eg, HIV infection, severe combined immune deficiency) are associated with infection following live vaccines. However, LAD does not impair response to live vaccines.

(Choice B) Deficiency of the terminal complement components (C5b-C9) results in an inability to form the complement membrane attack complex. This condition predisposes to recurrent infections by *Neisseria* organisms.

(Choice D) The absence of B lymphocytes in X-linked agammaglobulinemia leads to hypoplasia of lymphoid tissue, such as the tonsils or lymph nodes. However, both B cell number and function are normal in LAD.

(Choice E) Wiskott-Aldrich syndrome is an X-linked disorder characterized by the triad of thrombocytopenia, immunodeficiency, and eczema. It is caused by a defect in cytoskeleton rearrangement,





(Choice B) Deficiency of the terminal complement components (C5b-C9) results in an inability to form the complement membrane attack complex. This condition predisposes to recurrent infections by *Neisseria* organisms.

(Choice D) The absence of B lymphocytes in X-linked agammaglobulinemia leads to hypoplasia of lymphoid tissue, such as the tonsils or lymph nodes. However, both B cell number and function are normal in LAD.

(Choice E) Wiskott-Aldrich syndrome is an X-linked disorder characterized by the triad of thrombocytopenia, immunodeficiency, and eczema. It is caused by a defect in cytoskeleton rearrangement, not by CD18 deficiency.

Educational objective:

Leukocyte adhesion deficiency is due to absence of CD18 antigens necessary for the formation of integrins. Clinical features are caused by failure of leukocyte chemotaxis and include recurrent skin and mucosal infections without purulence, delayed separation of the umbilical cord, and persistent leukocytosis.

References

- [Disorders of neutrophil function: an overview.](#)





A 28-year-old woman comes to the clinic for follow-up after recent hospitalization due to autoimmune hepatitis. High-dose glucocorticoids improved the hepatitis, and on discharge, the patient continued prednisone therapy. Today, she feels well and has no other medical concerns. Physical examination shows no abdominal tenderness or jaundice. Prednisone is tapered and azathioprine is prescribed for continued management of autoimmune hepatitis. Which of the following should be periodically monitored while the patient is taking this new medication?

- ☐ A. Complete blood count
- ☐ B. Hemoglobin A1c
- ☐ C. Lipid panel
- ☐ D. Pulmonary function testing
- ☐ E. Vitamin B₁₂ level

Submit



A 28-year-old woman comes to the clinic for follow-up after recent hospitalization due to autoimmune hepatitis. High-dose glucocorticoids improved the hepatitis, and on discharge, the patient continued prednisone therapy. Today, she feels well and has no other medical concerns. Physical examination shows no abdominal tenderness or jaundice. Prednisone is tapered and azathioprine is prescribed for continued management of autoimmune hepatitis. Which of the following should be periodically monitored while the patient is taking this new medication?

- ☒ A. Complete blood count (85%)
- ☐ B. Hemoglobin A1c (2%)
- ☐ C. Lipid panel (5%)
- ☒ D. Pulmonary function testing (2%)
- ☐ E. Vitamin B₁₂ level (4%)

Incorrect

Correct answer



85%

Answered correctly



57 secs

Time Spent



10/20/2020

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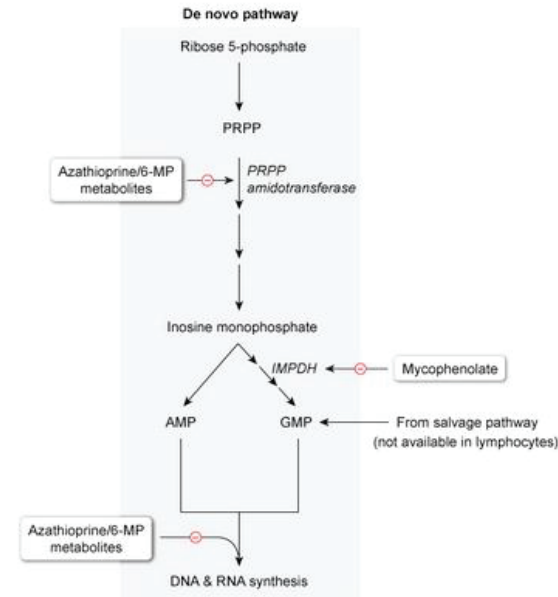


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Immunosuppressant inhibition of purine synthesis



6-MP = 6-mercaptopurine; AMP = adenosine monophosphate; GMP = guanosine monophosphate;
IMPDH = inosine monophosphate dehydrogenase; PRPP = phosphoribosyl pyrophosphate.

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6-MP = 6-mercaptopurine, AMP = adenosine monophosphate, GMP = guanosine monophosphate, IMPDH = inosine monophosphate dehydrogenase; PRPP = phosphoribosyl pyrophosphate.

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Azathioprine is an **immunosuppressant** used in the prevention of organ transplant rejection and the treatment of autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease, and autoimmune hepatitis. It functions via inhibition of purine synthesis pathways. Following ingestion, azathioprine is **converted** to 6-mercaptopurine, which is then converted to **6-thioguanine metabolites**; these metabolites are pharmacologically active and mediate both the therapeutic and adverse effects of azathioprine.

The 6-thioguanine metabolites reduce cellular proliferation via 2 methods of purine synthesis inhibition:

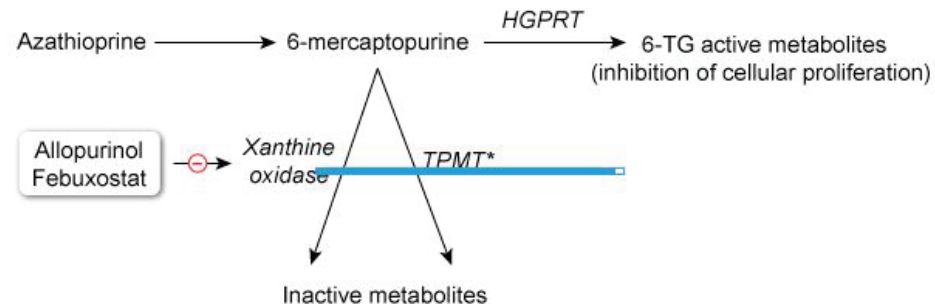
- The metabolites **inhibit** phosphoribosylpyrophosphate (**PRPP**) **amidotransferase**, an enzyme that catalyzes an early step in **de novo purine synthesis**.
- The metabolites act as **false nucleotides**, incorporating into actively replicating DNA and RNA and rendering the growing nucleic acid strand nonfunctional.

These effects are exerted preferentially on rapidly dividing cells (eg, activated lymphocytes in the setting of organ transplant or autoimmune disease) but are otherwise nonspecific and disrupt other hematologic cell lines, including neutrophils, erythrocytes, and platelets. Therefore, **pancytopenia** (ie, leukopenia, anemia,



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Azathioprine metabolism



*Genetic deficiency of TPMT is common

6-TG = 6-thioguanine; HGPRT = hypoxanthine-guanine phosphoribosyltransferase;

TPMT = thiopurine methyltransferase

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lines, including neutrophils, erythrocytes, and platelets. Therefore, **pancytopenia** (ie, leukopenia, anemia, and thrombocytopenia) is a common **adverse effect** that must be **monitored** with periodic **complete blood count** testing.

(Choices B and C) Unlike glucocorticoids, azathioprine has no adverse effects on glucose or lipid metabolism, an advantage of this medication over chronic glucocorticoid therapy.

(Choice D) Azathioprine has no known effect on lung function. The chemotherapeutic agent bleomycin may cause pulmonary fibrosis and therefore requires periodic monitoring of pulmonary function.

(Choice E) The anemia caused by azathioprine and other antimetabolite drugs (eg, methotrexate) is typically macrocytic (due to impaired DNA synthesis), but this macrocytic effect is independent of vitamin B₁₂ levels. Proton pump inhibitors and histamine 2 blockers can disrupt absorption of vitamin B₁₂ and may cause or contribute to its deficiency.

Educational objective:

Azathioprine is an immunosuppressant that functions via inhibition of purine synthesis by its pharmacologically active 6-thioguanine metabolites. In addition to the desired effect of reduced lymphocyte proliferation, the proliferation of other hematologic cell lines (eg, neutrophils, erythrocytes, platelets) is reduced, leading to a common adverse effect of pancytopenia.





A 14-year-old previously healthy girl is evaluated for a 3-month history of low back pain. She is a member of her school gymnastics team, and the pain is worse after training sessions. The patient reports no significant back trauma and has had no weakness or numbness in the lower extremities. Menarche was at age 9 and she has had regular menstruations. Vital signs are within normal limits. Physical examination shows tenderness in the L5 region, but no neurologic deficits are present. A spine x-ray reveals anterior displacement of L5 vertebra relative to the S1 vertebra. This patient's condition is most likely caused by injury to which of the following structures?

- ☐ A. Intervertebral disc
- ☐ B. Pars interarticularis
- ☐ C. Spinous process
- ☐ D. Transverse process
- ☐ E. Vertebral body

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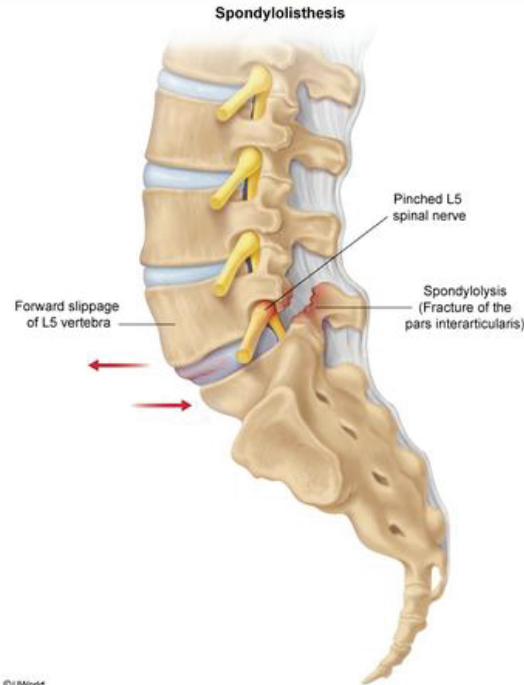


A 14-year-old previously healthy girl is evaluated for a 3-month history of low back pain. She is a member of her school gymnastics team, and the pain is worse after training sessions. The patient reports no significant back trauma and has had no weakness or numbness in the lower extremities. Menarche was at age 9 and she has had regular menstruations. Vital signs are within normal limits. Physical examination shows tenderness in the L5 region, but no neurologic deficits are present. A spine x-ray reveals anterior displacement of L5 vertebra relative to the S1 vertebra. This patient's condition is most likely caused by injury to which of the following structures?

- ☐ A. Intervertebral disc (36%)
- ☒ B. Pars interarticularis (35%)
- ☐ C. Spinous process (8%)
- ☐ D. Transverse process (7%)
- ☐ E. Vertebral body (11%)



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Spondylolisthesis



This adolescent athlete has spondylolisthesis (ie, anterior displacement of the vertebral body), which often occurs due to bilateral **spondylolysis** (ie, **pars interarticularis fracture**).

The vertebral column is formed by stacked vertebra separated by cartilaginous discs held together by thick ligaments:

- The **vertebral bodies** form the **anterior**, weight-bearing portion of the vertebral column.
- The posterior portion of the vertebral column contains the midline **spinous process**, the transverse processes, and the articulating processes of the facet joints.
- The **posterior vertebral arch** connects the anterior and posterior portions of the vertebral column and consists of the **pedicle**, the intervening **pars interarticularis**, and the **lamina**. The posterior vertebral arch and the posterior portion of the vertebral body form the triangularly shaped spinal canal.

Each vertebra has an anterior joint between the vertebral bodies separated by discs and a pair of facet joints posteriorly. Forward flexion of the spine stresses the anterior portion of the spine, including the vertebral bodies and discs; repetitive **extension of the spine** (as in gymnasts) stresses the facet joints and posterior vertebral arch, which can lead to spondylosis with subsequent spondylolisthesis.

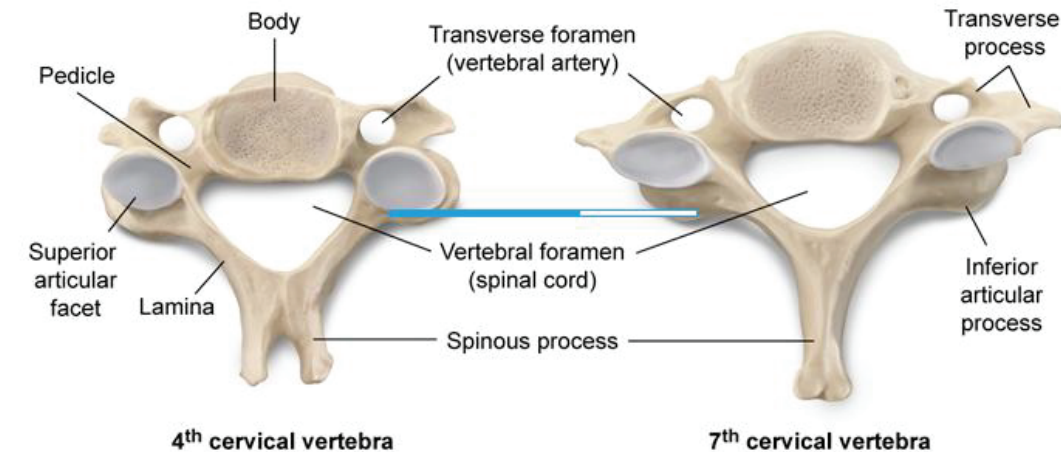
(Choice A) The intervertebral disc is a shock-absorbing cartilaginous structure between the vertebral bodies made of a tough cartilage ring (ie, annulus fibrosus) surrounding a soft fibrocartilaginous core (ie,



This adolescent athlete has spondylolisthesis (ie, anterior displacement of the vertebral body), which often

Exhibit Display

Cervical vertebral anatomy



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posterior vertebral arch, which can lead to spondylosis with subsequent spondylolisthesis.

(Choice A) The intervertebral disc is a shock-absorbing cartilaginous structure between the vertebral bodies made of a tough cartilage ring (ie, anulus fibrosis) surrounding a soft fibrocartilaginous core (ie, nucleus pulposus). Damage can lead to herniation of the disc or loss of space between the vertebral bodies but would not cause anterior displacement of the vertebral bodies.

(Choices C and D) The spinous process projects posteriorly in the midline and serves as an attachment of muscles and ligaments. The paired transverse processes project posterolaterally from the vertebral arch. In the thoracic vertebrae, facets on the transverse processes articulate with the tubercles of the ribs. Fractures of the spinous process or transverse processes are considered stable; they do not typically result in either neurologic compromise or displacement of the vertebral bodies.

(Choice E) The vertebral body is the weight-bearing, anterior portion of the vertebrae. Fractures to this area may cause avulsions or compression fractures that lead to a loss of height but not typically to displacement.

Educational objective:

Fracture of the posterior vertebral arch often occurs at the pars interarticularis (ie, spondylolysis). Bilateral disruption of the pars interarticularis can lead to anterior displacement of the vertebral body (ie,

bodies made of a tough cartilage ring (ie, anulus fibrosis) surrounding a soft fibrocartilaginous core (ie, nucleus pulposus). Damage can lead to herniation of the disc or loss of space between the vertebral bodies but would not cause anterior displacement of the vertebral bodies.

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Educational objective:

Fracture of the posterior vertebral arch often occurs at the pars interarticularis (ie, spondylolysis). Bilateral disruption of the pars interarticularis can lead to anterior displacement of the vertebral body (ie, spondylolisthesis).

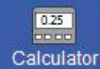
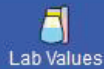


A muscle biopsy obtained from a healthy volunteer consists mainly of myoglobin-rich, glycogen-poor fibers with many mitochondria. Which of the following is the most likely biopsy site?

- ☐ A. Biceps brachii
- ☐ B. Deltoid
- ☐ C. Latissimus dorsi
- ☐ D. Paraspinal
- ☐ E. Pectoralis major

Submit





A muscle biopsy obtained from a healthy volunteer consists mainly of myoglobin-rich, glycogen-poor fibers with many mitochondria. Which of the following is the most likely biopsy site?

- ☐ A. Biceps brachii (16%)
- ☐ B. Deltoid (3%)
- ☐ C. Latissimus dorsi (6%)
- ☒ D. Paraspinal (70%)
- ☐ E. Pectoralis major (2%)

Correct



70%
Answered correctly



34 secs
Time Spent



12/29/2020
Last Updated

Explanation



**Muscle fiber characteristics**

| | Type I (slow twitch) | Type II (fast twitch) |
|------------------------------|-------------------------------|--|
| Action | Sustained force (eg, posture) | Rapid bursts (eg, heavy weightlifting) |
| Activity type | Endurance (aerobic) | Resistance (anaerobic) |
| Force generated | Low | High |
| Resistance to fatigue | High | Low |
| Lipid content | High | Low |
| Glycogen content | Low | High |
| Mitochondrial content | High | Low |
| Energy metabolism | Oxidative | Glycolytic |
| Color | Red (high myoglobin) | Pale red/white (low myoglobin) |
| Prototype | Soleus | Triceps |





The body's muscles are composed of 2 main fiber types: slow twitch (Type I) and fast twitch (Type II). **Type I fibers** perform actions requiring **low-level sustained force** (eg, postural maintenance) and function primarily via **aerobic metabolism**, meaning they have **high myoglobin** (oxygen storage) and **mitochondrial** (aerobic respiration) concentrations. The soleus muscle of the lower leg and paraspinal muscles of the back are postural muscles predominantly composed of Type I fibers.

Type II fibers are specialized for generating **rapid forceful** movements and they **fatigue quickly**. These fibers derive ATP energy mainly via glycogenolysis and subsequent **anaerobic glycolysis**. Muscles that maneuver the upper extremities (**Choices A, B, C, and E**) are primarily geared toward rapid forceful movements and are more likely to have a higher percentage of Type II than Type I muscle fibers.

Educational objective:

Postural skeletal muscles such as the soleus and paraspinal muscles contain predominantly Type I, slow twitch muscle fibers that derive ATP primarily via oxidative (aerobic) metabolism.

References

- [Exercise-induced skeletal muscle remodeling and metabolic adaptation: redox signaling and role of autophagy.](#)





As part of an experiment, radiolabeled ATP is injected into skeletal muscle. During muscle contraction, the labeled ATP is observed to attach to the sarcomere. This attachment causes immediate:

- ☐ A. Calcium binding to troponin C
- ☐ B. Tropomyosin displacement from the groove on the actin molecule
- ☐ C. Myosin head detachment from the actin filament
- ☐ D. Cross-bridge formation
- ☐ E. Myosin light chain phosphorylation by a specific enzyme

Submit






As part of an experiment, radiolabeled **ATP** is injected into skeletal muscle. During muscle contraction, the labeled ATP is observed to attach to the sarcomere. This attachment causes immediate:

- ☐ A. Calcium binding to troponin C (7%)
- ☐ B. Tropomyosin displacement from the groove on the actin molecule (7%)
- ☒ C. Myosin head detachment from the actin filament (70%)
- ☐ D. Cross-bridge formation (9%)
- ☐ E. Myosin light chain phosphorylation by a specific enzyme (4%)

Correct

 70%
Answered correctly

 59 secs
Time Spent

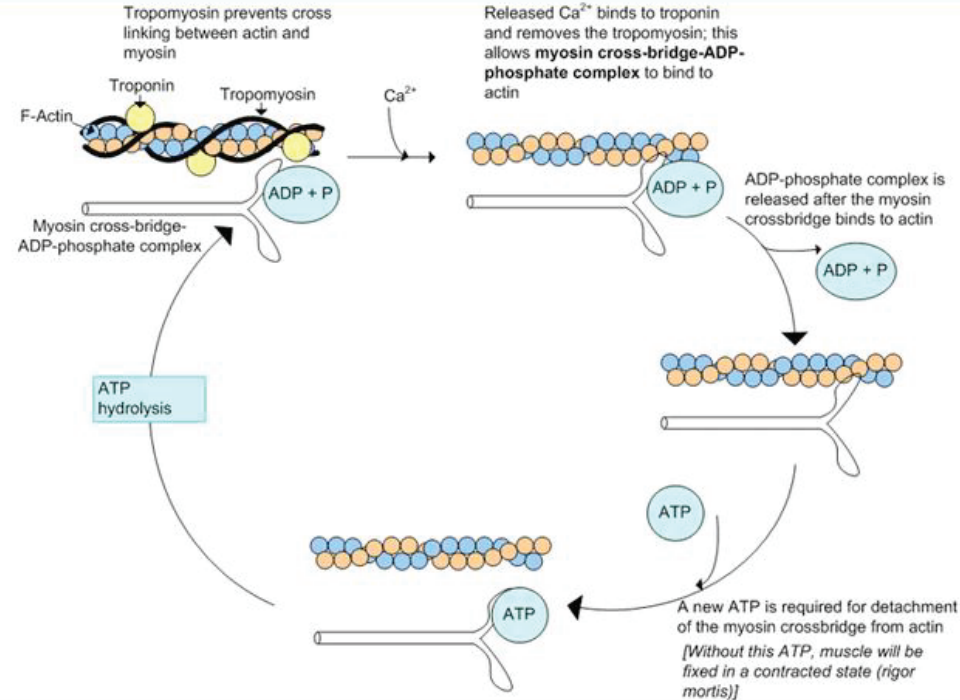
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Last Updated

Explanation





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mortis)]

According to the model posited by Rayment et al., the role of ATP in skeletal and cardiac muscle contraction may be to release the myosin head from its actin binding site and then to energize a conformational change that resets the myosin head to "contract" again the next time it binds to actin.

(Choices A and B) Calcium binding to troponin C shifts tropomyosin away from the myosin binding site on actin. These steps do not depend directly on ATP.

(Choice D) If ATP is not available, the cross-bridge between myosin and actin will persist (rigor mortis).

(Choice E) Myosin light chain kinase phosphorylates the myosin light chain, activating myosin to bind actin filaments in *smooth muscle* cells. There is no myosin head phosphorylation by a specific kinase in skeletal muscle contraction.

Educational Objective:

During the skeletal muscle contraction cycle, ATP binding to myosin causes release of the myosin head from its binding site on the actin filament.

Physiology
Subject

Rheumatology/Orthopedics & Sports
System

Muscle structure & physiology
Topic





A 35-year-old man comes to the clinic with acute right knee pain and swelling. His symptoms have been present for a week and have moderately worsened over this period. The patient is able to bear weight but has significant pain when climbing stairs or walking for extended distances. He attempted treatment with ibuprofen, which provided prompt but only temporary relief. Past medical history is unremarkable, though the patient was seen by his primary care provider for a diarrheal illness 2 weeks before onset of the current symptoms. Examination shows a moderate-sized effusion at the right knee. Cultures of a joint aspirate reveal no bacteria. Which of the following is most likely associated with this patient's joint symptoms?

- ☐ A. C1 inhibitor deficiency
- ☐ B. High titers of antistreptolysin O antibodies
- ☐ C. Histocompatibility antigen HLA-B27
- ☒ D. Positive serum antinuclear antibodies
- ☐ E. Positive serum rheumatoid factor

Submit



A 35-year-old man comes to the clinic with acute right knee pain and swelling. His symptoms have been present for a week and have moderately worsened over this period. The patient is able to bear weight but has significant pain when climbing stairs or walking for extended distances. He attempted treatment with ibuprofen, which provided prompt but only temporary relief. Past medical history is unremarkable, though the patient was seen by his primary care provider for a diarrheal illness 2 weeks before onset of the current symptoms. Examination shows a moderate-sized effusion at the right knee. Cultures of a joint aspirate reveal no bacteria. Which of the following is most likely associated with this patient's joint symptoms?

- ☐ A. C1 inhibitor deficiency (5%)
- ☐ B. High titers of antistreptolysin O antibodies (11%)
- ☒ C. Histocompatibility antigen HLA-B27 (71%)
- ☐ D. Positive serum antinuclear antibodies (6%)
- ☐ E. Positive serum rheumatoid factor (5%)





| Reactive arthritis | |
|-------------------------|--|
| Preceding infection | <ul style="list-style-type: none">• Genitourinary infection: <i>Chlamydia trachomatis</i>• Enteritis: <i>Salmonella, Shigella, Yersinia, Campylobacter, Clostridioides</i> (formerly <i>Clostridium</i>) <i>difficile</i> |
| Musculoskeletal | <ul style="list-style-type: none">• Asymmetric oligoarthritis• Enthesitis• Dactylitis |
| Extraarticular symptoms | <ul style="list-style-type: none">• Ocular: conjunctivitis, anterior uveitis• Genital: urethritis, cervicitis, prostatitis• Dermal: keratoderma blennorrhagicum, circinate balanitis• Oral ulcers |

This patient, a young man with acute lower extremity arthritis and a sterile joint effusion following a gastrointestinal infection, has typical symptoms of **reactive arthritis**. Reactive arthritis is a spondyloarthropathy that preferentially affects **HLA-B27-positive** individuals. It typically presents as an





• Oral ulcers

This patient, a young man with acute lower extremity arthritis and a sterile joint effusion following a gastrointestinal infection, has typical symptoms of **reactive arthritis**. Reactive arthritis is a spondyloarthropathy that preferentially affects **HLA-B27-positive** individuals. It typically presents as an asymmetric arthritis of the large joints. Common associated symptoms include conjunctivitis, urethritis, and [keratoderma blennorrhagicum](#).

Reactive arthritis is most common following infections with *Campylobacter*, *Shigella*, *Salmonella*, *Yersinia*, *Chlamydia*, or *Bartonella*. The clinical manifestations are caused by **immune complexes** involving bacterial antigens. However, it does not represent disseminated infection, and joint aspirates are sterile (ie, it is a 'reactive' not infectious arthritis).

(Choice A) C1 inhibitor deficiency is associated with hereditary angioedema. C1 inhibitor degrades C1 and prevents excessive complement activation and inflammation.

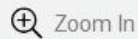
(Choice B) High titers of antistreptolysin O antibody are seen in nonpurulent complications of group A streptococcal infections, such as rheumatic fever and glomerulonephritis.

(Choices D and E) Antinuclear antibody and rheumatoid factor are nonspecific markers of autoimmune

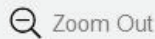




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It is a reactive not infectious arthritis).

(Choice A) C1 inhibitor deficiency is associated with hereditary angioedema. C1 inhibitor degrades C1 and prevents excessive complement activation and inflammation.

(Choice B) High titers of antistreptolysin O antibody are seen in nonpurulent complications of group A streptococcal infections, such as rheumatic fever and glomerulonephritis.

(Choices D and E) Antinuclear antibody and rheumatoid factor are nonspecific markers of autoimmune disease, primarily systemic lupus erythematosus and rheumatoid arthritis, respectively. These conditions are less common in men, do not usually present with acute monoarthritis, and are not associated with recent diarrheal illness.

Educational objective:

Reactive arthritis is a spondyloarthropathy associated with HLA-B27 that can occur following infection with *Chlamydia*, *Campylobacter*, *Salmonella*, *Shigella*, or *Yersinia*. It presents with sterile arthritis due to deposition of immune complexes.

References

- [Diagnosis and classification of reactive arthritis.](#)



A 48-year-old man comes to the office due to several hours of severe right knee pain. The patient has a history of peptic ulcer disease and gastroesophageal reflux disease. His right knee is swollen, erythematous, and tender. Arthrocentesis is performed and synovial fluid analysis shows needle-shaped, negatively birefringent crystals with many neutrophils. The medication given to this patient selectively binds to an interleukin-1 inducible enzyme that is highly expressed by inflammatory cells and undetectable in the surrounding normal tissue. Which of the following is most likely the drug used in this patient's treatment?

- ☐ A. Aspirin
- ☐ B. Celecoxib
- ☐ C. Colchicine
- ☐ D. Infliximab
- ☐ E. Prednisone

Submit

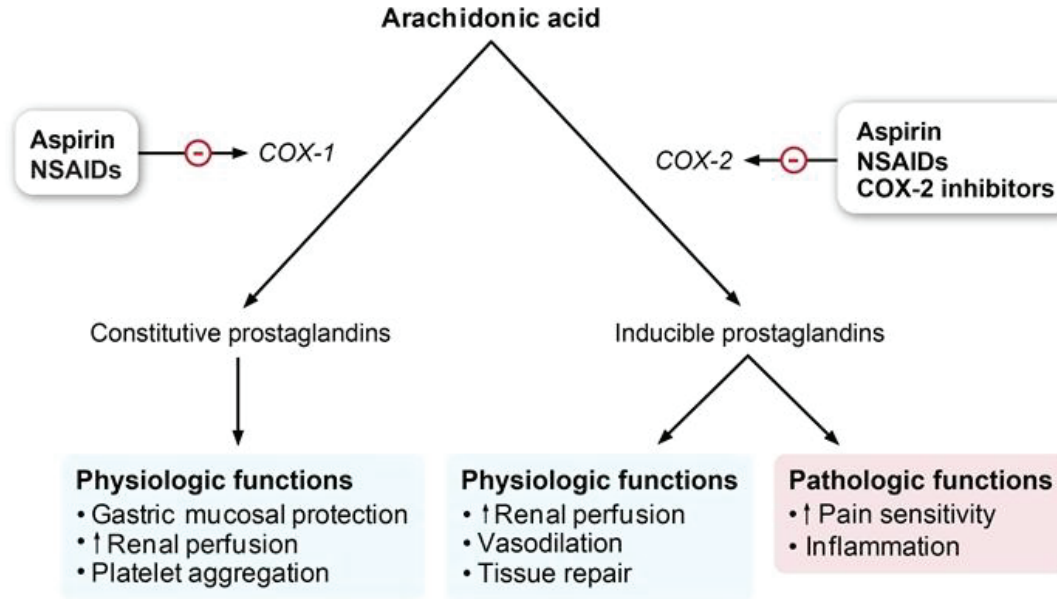


A 48-year-old man comes to the office due to several hours of severe right knee pain. The patient has a history of peptic ulcer disease and gastroesophageal reflux disease. His right knee is swollen, erythematous, and tender. Arthrocentesis is performed and synovial fluid analysis shows needle-shaped, negatively birefringent crystals with many neutrophils. The medication given to this patient selectively binds to an interleukin-1 inducible enzyme that is highly expressed by inflammatory cells and undetectable in the surrounding normal tissue. Which of the following is most likely the drug used in this patient's treatment?

- ☐ A. Aspirin (3%)
- ☒ B. Celecoxib (39%)
- ☐ C. Colchicine (20%)
- ☐ D. Infliximab (24%)
- ☐ E. Prednisone (12%)



Cyclooxygenase inhibitors



COX: cyclooxygenase NSAIDs: nonsteroidal anti-inflammatory drugs

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COX: cyclooxygenase, NSAIDs: nonsteroidal anti-inflammatory drugs

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Cyclooxygenase (COX), also known as prostaglandin endoperoxide synthase, catalyzes the conversion of arachidonic acid into prostanoids. It exists in 2 isoforms designated COX-1 and COX-2. COX-1 is constitutively expressed in various tissues and is involved in a number of "housekeeping functions" (eg, platelet aggregation, gastric mucosal protection, vascular homeostasis). **COX-2** is an **inducible** enzyme that is undetectable in most tissues under normal conditions. During **inflammation**, infiltrating cells secrete cytokines (eg, **interleukin-1**, **TNF- α**) that cause COX-2 upregulation in the inflamed tissue. COX-2 then drives the synthesis of pro-inflammatory **arachidonic acid metabolites**.

This patient's acute gout attack should be treated with an agent that provides prompt pain relief without exacerbating his gastrointestinal problems. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, indomethacin, and naproxen inhibit both COX-1 and COX-2 and can cause significant gastrointestinal injury. Selective **COX-2 inhibitors** (eg, celecoxib) decrease inflammation but have no effect on COX-1, minimizing gastroduodenal toxicity.

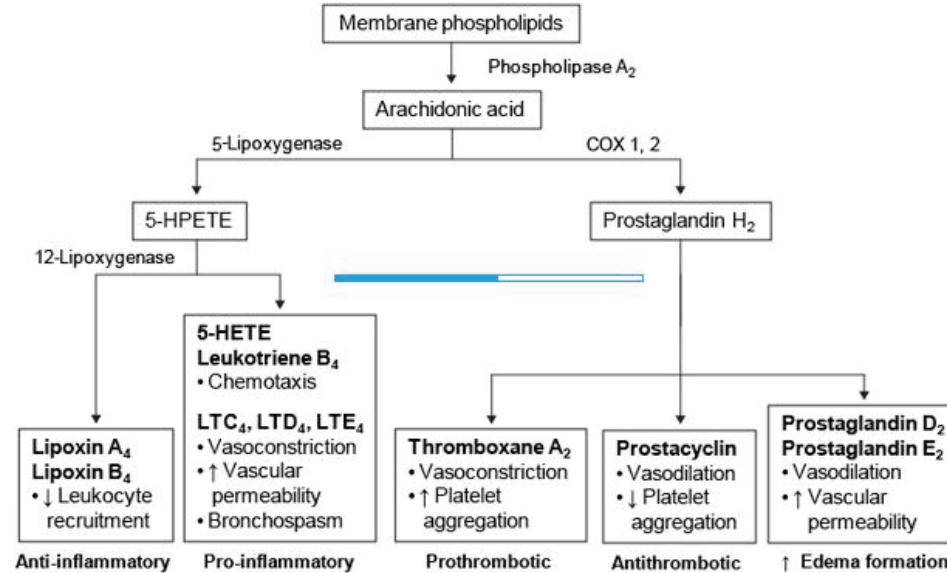
(Choice A) Like other NSAIDs, aspirin nonselectively inhibits both COX-1 and COX-2. Aspirin irreversibly modifies these enzymes; therefore, restoration of enzymatic activity requires synthesis of new enzymes.

(Choice C) Colchicine binds to tubulin, which inhibits microtubule formation. This results in impaired



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Arachidonic acid metabolic pathways



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(Choice A) Like other NSAIDs, aspirin nonselectively inhibits both COX-1 and COX-2. Aspirin irreversibly modifies these enzymes; therefore, restoration of enzymatic activity requires synthesis of new enzymes.

(Choice C) Colchicine binds to tubulin, which inhibits microtubule formation. This results in impaired neutrophil mitosis and decreased neutrophil chemotaxis.

(Choice D) Infliximab is a monoclonal antibody that irreversibly binds to and inhibits TNF- α , a cytokine involved in the inflammatory response. TNF- α is an intercellular signaling protein, not an enzyme.

(Choice E) Glucocorticoids (eg, prednisone) bind to cytoplasmic receptors that then translocate to the nucleus where the expression of anti-inflammatory peptides is upregulated. Glucocorticoids decrease COX-2 transcription but do not bind to COX-2 directly.

Educational objective:

Cyclooxygenase-2 (COX-2) is an inducible enzyme upregulated during inflammation by interleukin-1 and TNF- α . Selective COX-2 inhibitors (eg, celecoxib) decrease inflammation by inhibiting COX-2 production of pro-inflammatory arachidonic acid metabolites. Because they do not affect COX-1, they have minimal gastroduodenal toxicity.

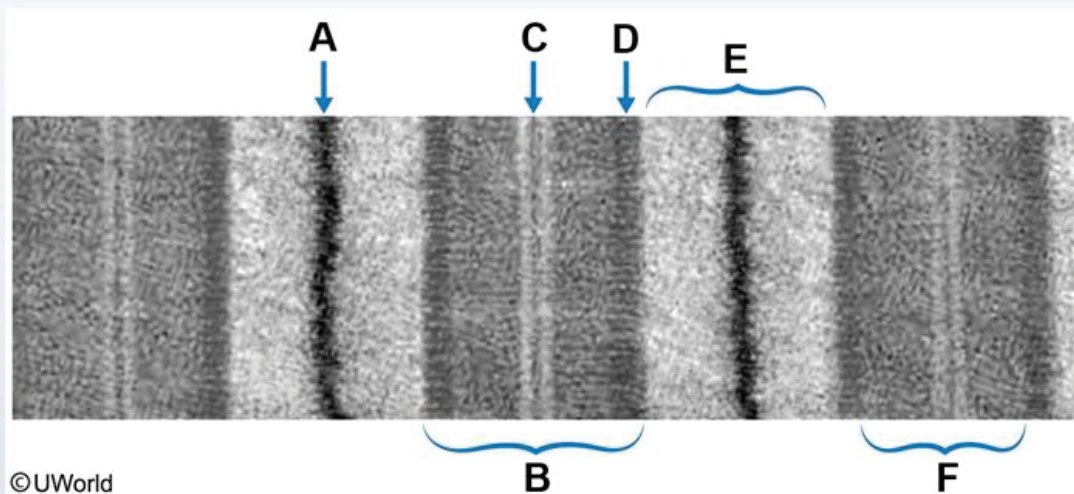
References

- Prostaglandins and inflammation.



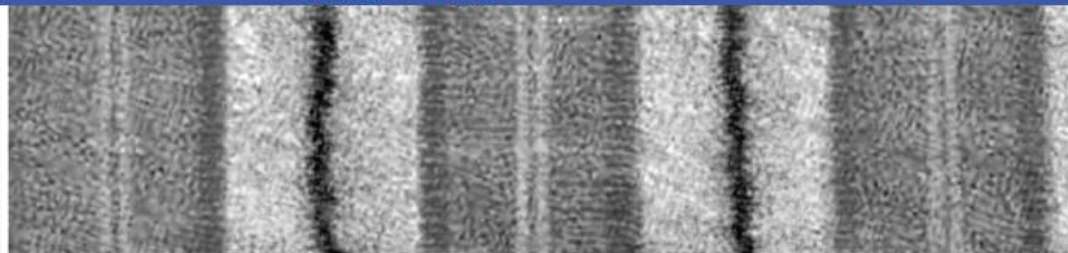


A researcher is investigating the structure of the sarcomere using skeletal muscle obtained from an experimental animal. He develops monoclonal antibodies directed against a specific skeletal muscle protein and finds that these antibodies disrupt the binding of actin to structural support elements within the sarcomere. Electron microscopy of the sarcomere is shown in the image below.



Which of the following labeled regions do these antibodies most likely bind?





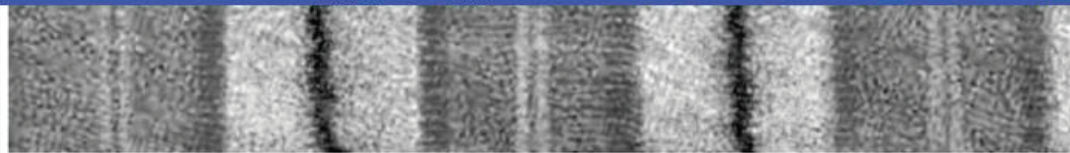
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B**F**

Which of the following labeled regions do these antibodies most likely bind?

- ☐ A. A
- ☐ B. B
- ☐ C. C
- ☐ D. D
- ☐ E. E
- ☐ F. F





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B

F

Which of the following labeled regions do these antibodies most likely bind?

✓ ☒ A.A (47%)

☐ B.B (8%)

☐ C.C (12%)

☐ D.D (15%)

☐ E.E (13%)

☐ F.F (3%)

Correct

47%

42 secs

03/08/2021

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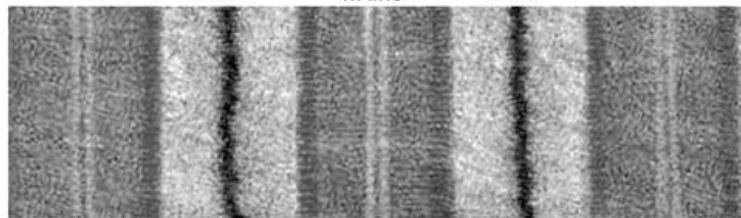
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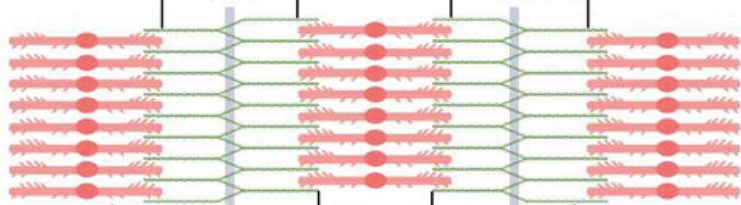
Exhibit Display

Sarcomere
(Z to Z)

Z line M line Z line



I band A band I band

Thick myofilament
(myosin)Thin myofilament
(actin)

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A **sarcomere** is composed of overlapping filaments of actin and myosin as well as structural and binding proteins (eg, titin, α -actinin). A single sarcomere is defined as the distance between two Z lines. **Thin (actin) filaments** are bound to structural proteins at the **Z line**. The unbound ends of the actin filaments project into the middle of the sarcomere, where they interact with thick (myosin) filaments during muscle contraction.

(Choice B) The A band corresponds to myosin filaments in the sarcomere. In this region, there are myosin filaments overlapped with actin filaments as well as non-overlapped myosin filaments. The A band always remains the same length during muscle contraction.

(Choice C) The M line lies at the center of the A band and is where myosin filaments anchor to structural elements in the center of the sarcomere.

(Choice D) Myosin and actin filaments overlap at the segment of the sarcomere between the H and I bands.

(Choices E and F) The I band is the region of the sarcomere in which actin does not overlap with myosin, and the H band is the region in which myosin does not overlap with actin. During muscle contraction, both H and I bands decrease in length.





always remains the same length during muscle contraction.

(Choice C) The M line lies at the center of the A band and is where myosin filaments anchor to structural elements in the center of the sarcomere.

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(Choices E and F) The I band is the region of the sarcomere in which actin does not overlap with myosin, and the H band is the region in which myosin does not overlap with actin. During muscle contraction, both H and I bands decrease in length.

Educational objective:

A single sarcomere is defined as the distance between two Z lines. Thin (actin) filaments in the I band are bound to structural proteins at the Z line, whereas thick (myosin) filaments in the A band are bound to structural proteins at the M line.

References

- [The muscle ultrastructure: a structural perspective of the sarcomere.](#)
- [The sarcomeric cytoskeleton: from molecules to motion.](#)

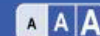




A 24-year-old woman comes to the office at 12 weeks gestation for prenatal counseling. She is 120 cm (3 ft 11 in) tall with short upper and lower extremities but normal torso length. Physical examination is also significant for depression of the nasal bridge and a bulging forehead. Her husband is phenotypically normal and has no medical problems. The patient knows that there is a 50% chance of passing on her condition to the fetus. An abnormality involving which of the following cells is most likely responsible for this patient's features?

- ☐ A. Chondrocytes
- ☐ B. Hypothalamic neurosecretory cells
- ☐ C. Osteoblasts
- ☐ D. Osteoclasts
- ☐ E. Pituitary somatotrophs

Submit



A 24-year-old woman comes to the office at 12 weeks gestation for prenatal counseling. She is 120 cm (3 ft 11 in) tall with short upper and lower extremities but normal torso length. Physical examination is also significant for depression of the nasal bridge and a bulging forehead. Her husband is phenotypically normal and has no medical problems. The patient knows that there is a 50% chance of passing on her condition to the fetus. An abnormality involving which of the following cells is most likely responsible for this patient's features?

- ☒ A. Chondrocytes (86%)
- ☐ B. Hypothalamic neurosecretory cells (2%)
- ☐ C. Osteoblasts (3%)
- ☐ D. Osteoclasts (1%)
- ☐ E. Pituitary somatotrophs (6%)

Correct



86%

Answered correctly



50 secs

Time Spent



03/04/2021

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Block Time Remaining: 00:18:42

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Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



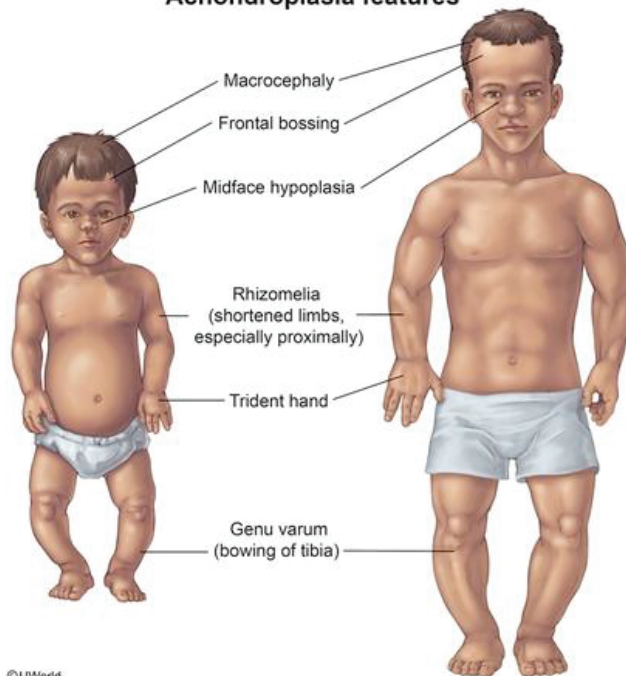
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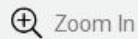
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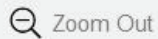
Achondroplasia features



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1



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This patient's limb shortening with normal torso length, specific craniofacial features (frontal bossing, midface hypoplasia), and risk of passing the condition to her offspring (50%) are characteristic of **achondroplasia**. The condition is caused by an autosomal dominant point mutation in the fibroblast growth factor receptor 3 (*FGFR3*) gene; 90% are de novo (unaffected parents) and 10% are inherited. Because the mutation is **autosomal dominant**, the fetus of an affected and an unaffected parent has a 50% chance of inheriting the mutation.

Achondroplasia affects **endochondral ossification**, the process that makes **long bones** (eg, humerus, femur, phalanges) and portions of the skull and face. In endochondral bone formation, mesenchymal cells differentiate into chondrocytes that secrete cartilage matrix. These chondrocytes continue to proliferate through childhood, forming an elongating cartilage template that progressively becomes calcified and later invaded by osteoblasts, osteoclasts, and blood vessels originating from the periosteum. Deposition of osteoid matrix over the septa of calcified cartilage matrix forms woven bone, which then undergoes remodeling into compact bone.

FGFR3 is normally responsible for limiting chondrocyte proliferation during endochondral ossification. In achondroplasia, FGFR3 becomes constitutively activated, causing exaggerated **inhibition of chondrocyte**





FGFR3 is normally responsible for limiting chondrocyte proliferation during endochondral ossification. In achondroplasia, FGFR3 becomes constitutively activated, causing exaggerated **inhibition of chondrocyte proliferation** that results in the characteristic bone shortening and craniofacial abnormalities.

(Choices B and E) Hypothalamic neurosecretory cells produce growth hormone-releasing hormone and anterior pituitary somatotrophs produce growth hormone (GH). Hypothalamic or pituitary insults (eg, tumor, ischemia) can result in defective release of either hormone. GH deficiency can lead to proportional short stature (both long and flat bones affected) as opposed to the disproportionate short stature seen in achondroplasia (only long bones affected).

(Choice C) The flat bones (eg, most of the skull, pelvis) grow primarily via intramembranous (not endochondral) ossification. In intramembranous ossification, mesenchymal cells differentiate directly into osteoblasts and begin osteoid matrix secretion without the formation of cartilaginous bones. As a result, most flat bones remain unaffected in achondroplasia.

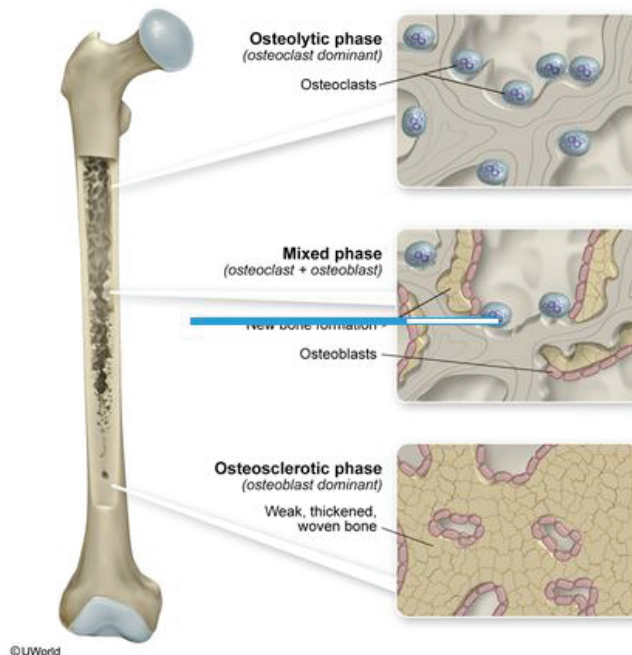
(Choice D) Osteoclasts are specialized macrophages that function to resorb bone. [Paget disease](#), characterized by disordered bone mass, initially begins with excessive activity of abnormally large osteoclasts followed by osteoblastic activity and eventual sclerosis. Patients are usually elderly and can present with focal bone pain and pathologic fractures.



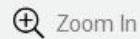


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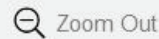
Paget disease of bone



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present with focal bone pain and pathologic fractures

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achondroplasia (only long bones affected).

(Choice C) The flat bones (eg, most of the skull, pelvis) grow primarily via intramembranous (not endochondral) ossification. In intramembranous ossification, mesenchymal cells differentiate directly into osteoblasts and begin osteoid matrix secretion without the formation of cartilaginous bones. As a result, most flat bones remain unaffected in achondroplasia.

(Choice D) Osteoclasts are specialized macrophages that function to resorb bone. [Paget disease](#), characterized by disordered bone mass, initially begins with excessive activity of abnormally large osteoclasts followed by osteoblastic activity and eventual sclerosis. Patients are usually elderly and can present with focal bone pain and pathologic fractures.

Educational objective:

Unlike the process of intramembranous ossification that forms flat bones, endochondral ossification proceeds along a cartilage template and is responsible for the formation of long bones. Achondroplasia is characterized by an exaggerated inhibition of chondrocyte proliferation in the growth plates of long bones and manifests with proximal limb shortening, midface hypoplasia, and macrocephaly.

References

- [Pediatric aspects of skeletal dysplasia.](#)



A 34-year-old woman comes to the office with several months of vision problems, difficulty chewing, and trouble speaking. The symptoms fluctuate, but the patient has noticed that they are worse after a long day. She works as a telemarketer and has been putting in increasingly long hours to meet her quotas. Regarding her symptoms, she says, "It's probably just exhaustion; an ice pack to my face seems to help." During physical examination, the patient is asked to keep her eyes focused on a spot on the ceiling, and after 2 minutes, her vision becomes blurry. The remainder of the examination is normal. Further evaluation shows that the patient's symptoms are reversible on administration of an acetylcholinesterase inhibitor. The pathogenesis of this patient's disease is most similar to which of the following conditions?

- ☐ A. Atopic dermatitis
- ☐ B. Contact dermatitis
- ☐ C. Goodpasture syndrome
- ☐ D. Hypersensitivity pneumonitis
- ☐ E. Postinfectious glomerulonephritis





trouble speaking. The symptoms fluctuate, but the patient has noticed that they are worse after a long day.

She works as a telemarketer and has been putting in increasingly long hours to meet her quotas.

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During physical examination, the patient is asked to keep her eyes focused on a spot on the ceiling, and

after 2 minutes, her vision becomes blurry. The remainder of the examination is normal. Further evaluation

shows that the patient's symptoms are reversible on administration of an acetylcholinesterase inhibitor.

The pathogenesis of this patient's disease is most similar to which of the following conditions?

- ☐ A. Atopic dermatitis (3%)
- ☐ B. Contact dermatitis (3%)
- ☒ C. Goodpasture syndrome (82%)
- ☐ D. Hypersensitivity pneumonitis (3%)
- ☐ E. Postinfectious glomerulonephritis (6%)

Correct

82%



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12/27/2020

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This patient's clinical findings of intermittent diplopia, difficulty chewing, and speech problems (especially at the end of the day) suggest a diagnosis of **myasthenia gravis** (MG). MG is caused by impaired functioning of nicotinic cholinergic receptors at the neuromuscular junction due to interference by **IgG autoantibodies**. The diagnosis can be confirmed with administration of an anticholinesterase agent (eg, edrophonium), which increases the amount of acetylcholine at the neuromuscular junction. Acetylcholinesterase activity decreases at lower temperatures, so application of an ice pack can also improve symptoms caused by weakness of superficial muscles (eg, ptosis).

MG is a form of **type II hypersensitivity**, which is characterized by IgM and/or IgG autoantibodies that bind to cell surface antigens and/or extracellular matrix components. Among the available options, only Goodpasture syndrome is due to the production of autoantibodies (directed against the glomerular basement membrane). These antibodies cause inflammatory destruction of the basement membrane in the lung alveoli and renal glomeruli.

(Choice A) Atopic dermatitis is a chronic, pruritic, eczematous skin condition that almost always begins in childhood. The pathogenicity involves several factors, including skin barrier abnormalities, defects in innate immunity, and a T_H2 -skewed immune response.

(Choice B) The pathogenesis of contact dermatitis (type IV hypersensitivity reaction) involves cutaneous



(Choice B) The pathogenesis of contact dermatitis (type IV hypersensitivity reaction) involves cutaneous exposure to small foreign molecules (haptens) that bind to skin proteins. These proteins are subsequently processed by antigen-presenting Langerhans cells that transport the modified proteins to lymph nodes and promote the development of hapten-specific T cells. With continued hapten exposure, sensitized T cells produce inflammatory cytokines at the exposure site, causing the characteristic eczematous skin changes.

(Choice D) Most patients with acute hypersensitivity pneumonitis have specific serum IgG antibodies that precipitate bacterial or fungal antigens found in inhaled organic dust particles. This causes interstitial alveolitis and bronchiolitis via immune complex and complement deposition in vessel walls (type III hypersensitivity mechanism).

(Choice E) The pathogenesis of poststreptococcal glomerulonephritis involves granular deposition of immune complexes containing group A streptococcal antigens, IgG, and C3 in the glomerular basement membrane and mesangium. It is a type III, immune complex-mediated, hypersensitivity response.

Educational objective:

Myasthenia gravis results from an autoimmune type II (antibody-mediated) hypersensitivity reaction against skeletal myocyte surface acetylcholine receptors. Goodpasture syndrome similarly involves autoantibodies against basement membrane collagen in the renal glomeruli and lung alveoli.





A 55-year-old nurse was started on multidrug therapy 3 weeks ago to treat pulmonary tuberculosis contracted from a former patient. He comes to his primary care provider due to fatigue and low-grade fever for several days. He also has had muscle aches and severe joint pain in his elbows, wrists, and knees. The patient says, "I don't think it's the flu; I had the vaccine months ago." He has no current respiratory symptoms apart from pleuritic chest pain. The patient has no other significant past medical or family history. His examination is unremarkable. Laboratory results are as follows:

| | |
|---------------------|-------------------------|
| Hemoglobin | 12.6 g/dL |
| Platelets | 120,000/mm ³ |
| Leukocytes | 11,000/mm ³ |
| Blood urea nitrogen | 18 mg/dL |
| Creatinine | 0.8 mg/dL |
| Anti-histone | positive |





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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Creatinine 0.8 mg/dL

Anti-histone
antibody positive

Anti-nuclear
antibody positive

An abnormality in which of the following metabolic processes most likely underlies this patient's current condition?

- ☐ A. Liver acetylation
- ☐ B. Liver hydrolysis
- ☐ C. Liver hydroxylation
- ☐ D. Liver sulfate conjugation
- ☐ E. Plasma hydrolysis
- ☐ F. Unchanged excretion



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antibody

positive

Anti-nuclear
antibody

positive

An abnormality in which of the following metabolic processes most likely underlies this patient's current condition?



- ☒ A. Liver acetylation (65%)
- ☐ B. Liver hydrolysis (5%)
- ☐ C. Liver hydroxylation (14%)
- ☐ D. Liver sulfate conjugation (9%)
- ☐ E. Plasma hydrolysis (2%)
- ☐ F. Unchanged excretion (2%)





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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Text Zoom

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Features of drug-induced lupus erythematosus

| | |
|---------------------|---|
| Clinical features | <ul style="list-style-type: none">• Abrupt-onset symptoms<ul style="list-style-type: none">○ Fever/fatigue○ Arthralgias/arthritis○ Rash○ Serositis• Predilection for slow acetylators |
| Laboratory findings | <ul style="list-style-type: none">• Anti-histone antibodies present in >95% of patients• Anti-dsDNA antibodies rarely seen (specific for systemic lupus erythematosus) |
| Implicated drugs | <ul style="list-style-type: none">• Procainamide• Hydralazine• Isoniazid• Minocycline• TNF-α inhibitors (eg, etanercept) |

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This patient's clinical findings (constitutional symptoms, arthralgias, and pleuritic chest pain), **anti-histone**

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This patient's clinical findings (constitutional symptoms, arthralgias, and pleuritic chest pain), **anti-histone antibodies**, and recent **isoniazid** use support the diagnosis of **drug-induced lupus erythematosus** (DILE). Unlike classic lupus, DILE typically lacks the usual cutaneous manifestations (eg, malar rash) and is rarely associated with neurologic or renal complications. Clinical improvement is rapid on discontinuation of the causative agent.

Procainamide, hydralazine, and isoniazid are metabolized via phase II **acetylation** in the liver. Hepatic expression of N-acetyltransferase is genetically determined, and patients with a slow acetylator phenotype are at greater risk of developing DILE. Patients who are slow acetylators are also predisposed to isoniazid-induced peripheral neuropathy due to increased drug concentrations.

(Choice B) Liver hydrolysis is a phase I reaction in which a compound is cleaved by adding water (eg, esterase or amidase enzymes). Phase I metabolism usually precedes phase II conjugation metabolism.

(Choice C) Liver hydroxylation is a phase I oxidation transformation catalyzed by the cytochrome P450 monooxygenase system. Addition of a hydroxyl group reduces lipid solubility and facilitates excretion.

(Choice D) Liver sulfate conjugation is a phase II metabolic pathway that biotransforms drugs into more polar compounds that are more water soluble and easily excreted.



monooxygenase system. Addition of a hydroxyl group reduces lipid solubility and facilitates excretion.

(Choice D) Liver sulfate conjugation is a phase II metabolic pathway that biotransforms drugs into more polar compounds that are more water soluble and easily excreted.

(Choice E) Certain drugs are hydrolyzed by plasma esterases, which rapidly cleave ester linkages after the drug enters the circulation. This rapid inactivation allows for the short duration of action of these medications. Many drugs used in anesthesia (eg, succinylcholine, tetracaine, remifentanyl) are metabolized by plasma hydrolysis.

(Choice F) A few drugs are not metabolized in the body. They are excreted in the urine mostly unchanged and are still pharmacologically active.

Educational objective:

Drug-induced lupus erythematosus (DILE) is characterized by abrupt onset of lupus symptoms (eg, fever, arthralgias, pleuritis) with positive anti-histone antibodies. It has been linked to drugs metabolized by N-acetylation in the liver (eg, procainamide, hydralazine, isoniazid). Genetically predisposed individuals who are slow acetylators are at greater risk for developing DILE.

Pharmacology Rheumatology/Orthopedics & Sports SLE

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A 48-year-old previously healthy woman comes to the office due to progressively worsening muscle weakness for the past 2 months. The patient has difficulty with activities such as climbing stairs, getting up from chairs, and placing dishes in overhead cabinets. She also reports a 4.5-kg (10-lb) unintentional weight loss and occasional abdominal discomfort over the same interval. Physical examination shows weakness of the shoulder and hip girdle muscles. Other examination findings are shown in the image below.





Item 19 of 40

Question Id: 11805



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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below.

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Further evaluation of this patient is most likely to reveal which of the following associated conditions?

- ☐ A. Chronic hepatitis C infection
- ☐ B. Ovarian adenocarcinoma
- ☐ C. Primary biliary cholangitis
- ☐ D. *Tropheryma whippelii* infection
- ☐ E. Type 2 diabetes mellitus

Submit

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Further evaluation of this patient is most likely to reveal which of the following associated conditions?

- ☐ A. Chronic hepatitis C infection (10%)
- ☒ B. Ovarian adenocarcinoma (40%)
- ☐ C. Primary biliary cholangitis (34%)
- ☐ D. *Tropheryma whippelii* infection (10%)
- ☐ E. Type 2 diabetes mellitus (4%)

Correct

40%



02 mins, 01 sec



02/26/2021

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Dermatomyositis is a systemic autoimmune disease characterized by proximal muscle weakness resembling polymyositis, with additional inflammatory features involving the skin. Specific skin findings include the **heliotrope rash** in the periorbital area and cheeks and **Gotttron papules**, which are raised erythematous plaques over the joints and bony prominences of the hands (as seen in this patient). Muscle biopsy is diagnostic and shows mononuclear **perifascicular inflammation** and atrophy (ie, occurring along the periphery of the fascicles).

Dermatomyositis may occur alone or as a **paraneoplastic syndrome** of an underlying malignancy, most commonly due to underlying **adenocarcinoma** (eg, ovary, lung, pancreas). Symptoms may precede the diagnosis of malignancy but often parallel the course of the cancer.

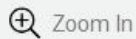
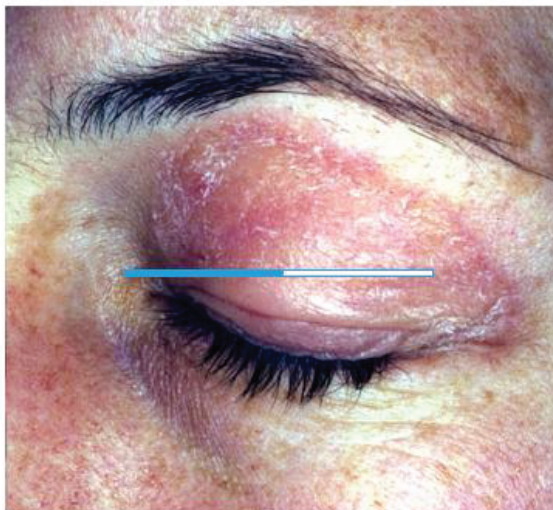
(Choice A) Hepatitis C infection is associated with porphyria cutanea tarda, which presents with skin fragility and a **blistering rash** in sun-exposed areas, and mixed cryoglobulinemic vasculitis, which presents with nonblanching palpable purpura. Muscle symptoms are not typical.

(Choice C) Primary biliary cholangitis (previously primary biliary cirrhosis) is an autoimmune liver disease that can present with cholestasis, malabsorption, pruritus, and jaundice. Although the risk of this condition is increased in patients with autoimmune disease (eg, CREST syndrome, Sjögren syndrome), the association with dermatomyositis is not common.

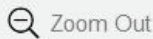




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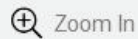


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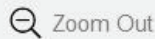




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with nonblanching palpable purpura. Muscle symptoms are not typical.

(Choice C) Primary biliary cholangitis (previously primary biliary cirrhosis) is an autoimmune liver disease that can present with cholestasis, malabsorption, pruritus, and jaundice. Although the risk of this condition is increased in patients with autoimmune disease (eg, CREST syndrome, Sjögren syndrome), the association with dermatomyositis is not common.

(Choice D) *Tropheryma whippelii* infection (Whipple disease) typically presents with arthritis, diarrhea, and fever. Patients may develop hyperpigmentation, but skin and muscle symptoms are otherwise not prominent.

(Choice E) Type 2 diabetes is due to insulin resistance, which may also cause *acanthosis nigricans*, a condition characterized by velvety patches of brownish discoloration affecting the neck and skinfolds.

Educational objective:

Dermatomyositis is characterized by proximal muscle weakness resembling polymyositis, with additional inflammatory features involving the skin (heliotrope rash, Gottron papules). Both dermatomyositis and polymyositis may occur alone or as a paraneoplastic syndrome associated with an underlying adenocarcinoma (eg, ovary, lung, pancreas).

References



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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with nonblanching palpable purpura. Muscle symptoms are not typical.

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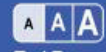
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A 34-year-old man develops severe chest and abdominal pain while shopping in a mall. Paramedics arrive and find him in severe distress. Several minutes later, he suffers a cardiac arrest with pulseless electrical activity and cannot be resuscitated. Postmortem examination reveals an internal hemorrhage as the cause of death. Histochemical evaluation of the patient's tissues reveals a defect affecting a large extracellular glycoprotein. This protein is normally found abundantly in large blood vessels, periosteum, and zonular fibers of the lens and functions to form microfibrils by surrounding elastin. This patient most likely suffered from which of the following conditions?

- ☐ A. Ehlers-Danlos syndrome
- ☐ B. Homocystinuria
- ☐ C. Marfan syndrome
- ☐ D. Osteogenesis imperfecta
- ☐ E. Polycystic kidney disease
- ☐ F. Vitamin C deficiency





and find him in severe **distress**. Several minutes later, he suffers a **cardiac arrest** with pulseless electrical activity and cannot be resuscitated. Postmortem examination reveals an **internal hemorrhage** as the cause of death. Histochemical evaluation of the patient's tissues reveals a defect affecting a **large extracellular glycoprotein**. This protein is normally found abundantly in large blood vessels, periosteum, and zonular fibers of the lens and functions to form microfibrils by surrounding elastin. This patient most likely suffered from which of the following conditions?

- ☐ A. Ehlers-Danlos syndrome (15%)
- ☐ B. Homocystinuria (1%)
- ☒ C. Marfan syndrome (80%)
- ☐ D. Osteogenesis imperfecta (1%)
- ☐ E. Polycystic kidney disease (0%)
- ☐ F. Vitamin C deficiency (0%)

Correct

80%
Answered correctly01 min, 25 secs
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Clinical features of Marfan syndrome

| | |
|-----------------------|--|
| Skeletal | <ul style="list-style-type: none">• Arachnodactyly• ↓ Upper-to-lower body segment ratio, ↑ arm-to-height ratio• Pectus deformity, scoliosis, or kyphosis• Joint hypermobility |
| Ocular | <ul style="list-style-type: none">• Ectopia lentis |
| Cardiovascular | <ul style="list-style-type: none">• Aortic dilation, regurgitation, or dissection• Mitral valve prolapse |
| Pulmonary | <ul style="list-style-type: none">• Spontaneous pneumothorax from apical blebs |
| Skin | <ul style="list-style-type: none">• Recurrent or incisional hernia• Skin striae |

Fibrillin-1 is a major component of microfibrils that form a sheath around elastin fibers. Microfibrils are abundant in blood vessels (eg, aortic media), periosteum, and the suspensory ligaments of the lens.

Fibrillin in the extracellular space acts as a scaffold for deposition of elastin extruded from connective tissue



Fibrillin-1 is a major component of microfibrils that form a sheath around elastin fibers. Microfibrils are abundant in blood vessels (eg, aortic media), periosteum, and the suspensory ligaments of the lens. Fibrillin in the extracellular space acts as a scaffold for deposition of elastin extruded from connective tissue cells. Defects in fibrillin-1 cause mechanical weakening in the connective tissues and abnormal activation of transforming growth factor beta.

Marfan syndrome is caused by an inherited defect in the fibrillin-1 gene. Patients with Marfan syndrome can often be identified due to a characteristic **body habitus**, with long thin extremities, loose joints, and long fingers (arachnodactyly). The cause of death in Marfan syndrome is most often due to cardiovascular complications (eg, **aortic root dilation, dissection, and rupture**).

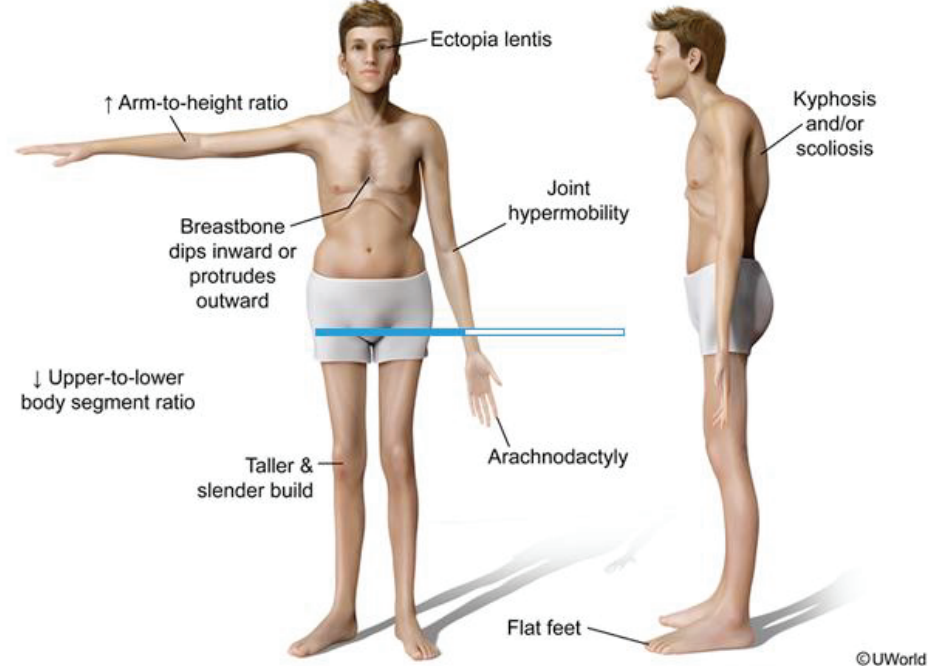
(Choice A) Ehlers-Danlos syndrome is a collection of heritable disorders of connective tissue characterized by skin and joint hypermobility. Like those with Marfan syndrome, these patients are at risk for aortic rupture. However, Ehlers-Danlos syndrome affects the formation and extracellular structuring of collagen rather than microfibrils.

(Choice B) Homocystinuria is a rare inherited metabolic disorder due to cystathionine synthase deficiency. It is characterized by very high circulating homocysteine levels, marfanoid habitus, and increased risk for premature atherosclerotic cardiovascular disease.

Fibrillin-1 is a major component of microfibrils that form a sheath around elastin fibers. Microfibrils are

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Marfanoid habitus



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deficiency. It is characterized by very high circulating homocysteine levels, marfanoid habitus, and increased risk for premature atherosclerotic cardiovascular disease.

(Choice D) Osteogenesis imperfecta results from defects in the genes encoding type I collagen, a major component of bones. Defects in type I collagen in osteogenesis imperfecta result in reduced bone mass and fragility fractures. Other manifestations of the disease include blue sclera, dental abnormalities, and hearing loss.

(Choice E) Autosomal dominant polycystic kidney disease is a disorder of tubular epithelial cells. It causes enlargement of the kidneys with numerous parenchymal cysts. Patients are also at risk for cardiac valvular disorders and ruptured cerebral aneurysms.

(Choice F) Deficiency of vitamin C (scurvy) causes impaired hydroxylation of proline and lysine residues in collagen. Clinical features include skin fragility, easy bleeding, and poor dentition.

Educational objective:

Marfan syndrome is due to a defect in fibrillin-1, an extracellular glycoprotein that acts as a scaffold for elastin. It is abundant in the zonular fibers of the lens, periosteum, and aortic media. Aortic root dilation with dissection and rupture is a common cause of death.

References





A 48-year-old woman comes to the office due to difficulty swallowing dry foods such as crackers. She has no pain during swallowing or heartburn. The patient is a college professor and has to drink water frequently during lectures to keep her mouth moist. She also reports a gritty sensation in her eyes, which is often worse in the evening, and occasional brief episodes of joint pain. Medical history is significant for hypothyroidism, for which she takes levothyroxine. Physical examination shows mild conjunctival erythema and cracking of the lips. There is diffuse, nontender thyroid enlargement, which is unchanged from prior examination. The remainder of the examination is normal. Biopsy of the lip mucosa is most likely to reveal which of the following findings?

- ☐ A. Extracellular deposition of amorphous proteins
- ☐ B. Hyperkeratosis and dysplasia limited to the epithelium
- ☐ C. Intraepidermal spongiosis and acantholysis
- ☐ D. Periductal lymphocytic infiltration of labial glands
- ☐ E. Scattered, noncaseating, epithelioid granulomas





no pain during swallowing or heartburn. The patient is a college professor and has to drink water frequently during lectures to keep her mouth moist. She also reports a gritty sensation in her eyes, which is often worse in the evening, and occasional brief episodes of joint pain. Medical history is significant for hypothyroidism, for which she takes levothyroxine. Physical examination shows mild conjunctival erythema and cracking of the lips. There is diffuse, nontender thyroid enlargement, which is unchanged from prior examination. The remainder of the examination is normal. Biopsy of the lip mucosa is most likely to reveal which of the following findings?

- ☐ A. Extracellular deposition of amorphous proteins (6%)
- ☐ B. Hyperkeratosis and dysplasia limited to the epithelium (9%)
- ☐ C. Intraepidermal spongiosis and acantholysis (4%)
- ☒ D. Periductal lymphocytic infiltration of labial glands (73%)
- ☐ E. Scattered, noncaseating, epithelioid granulomas (6%)

Correct



73%

Answered correctly



01 min, 19 secs

Time spent



03/09/2021

Last updated

Block Time Remaining: 00:25:55

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Previous



Next



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Tutorial



Lab Values



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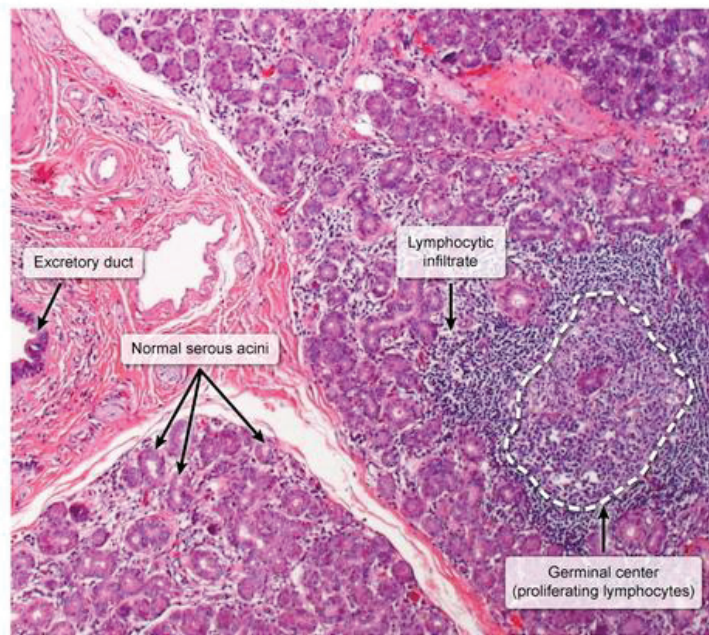
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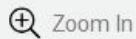
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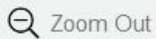
Sjogren syndrome



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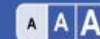
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Sjögren syndrome is an autoimmune disorder characterized by inflammation of exocrine (eg, salivary, lacrimal) glands. It can occur as an isolated disorder or as a manifestation of another autoimmune syndrome (eg, rheumatoid arthritis). Patients typically have severe dry mouth (**xerostomia**) and dry eyes (**keratoconjunctivitis sicca**); vaginal gland involvement is also common.

Characteristic serologic markers of Sjögren syndrome include **anti-Ro (SSA)** and **anti-La (SSB)**.

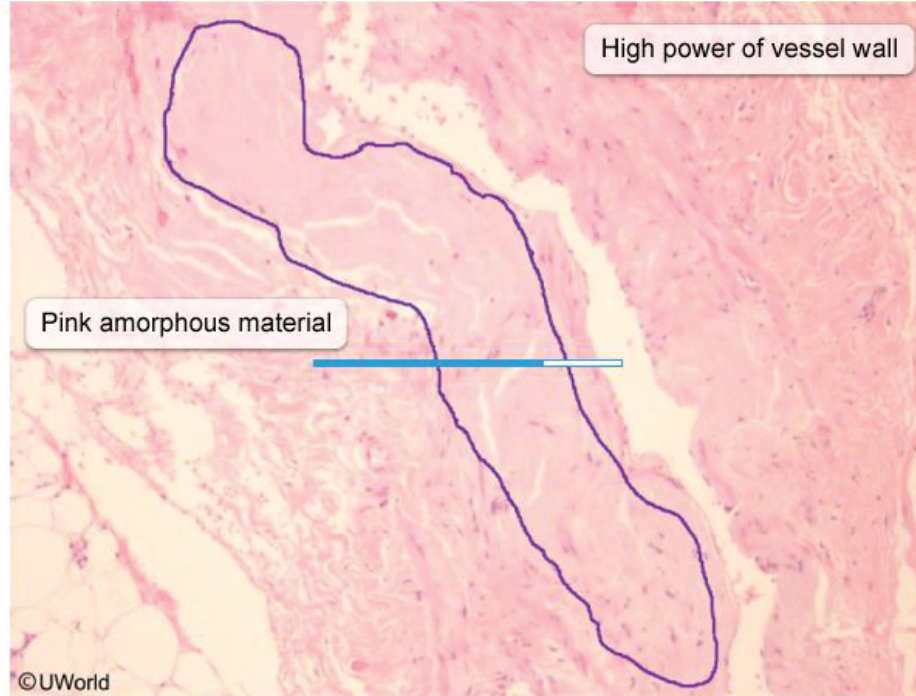
Antinuclear antibodies and rheumatoid factor are often positive but less specific. Biopsy of the labial salivary glands demonstrates intense **periductal lymphocytic infiltrates** (focal lymphocytic sialadenitis), often with germinal centers; the glandular tissue is typically atrophic and fibrotic.

(Choice A) Amyloidosis is a group of disorders characterized by deposition of abnormal proteins in various tissues (eg, kidneys, heart). Light microscopy shows amorphous **eosinophilic protein deposits**; polarized microscopy with Congo red staining may elicit **bright green birefringence**.

(Choice B) Oral leukoplakia is a premalignant lesion characterized by hyperplasia of the squamous mucosa. The hyperkeratinized patches appear white against the normal red or pink mucosa. In the absence of malignant transformation, these lesions are typically asymptomatic; this patient's dry mouth and dry eye symptoms are more consistent with Sjögren syndrome.

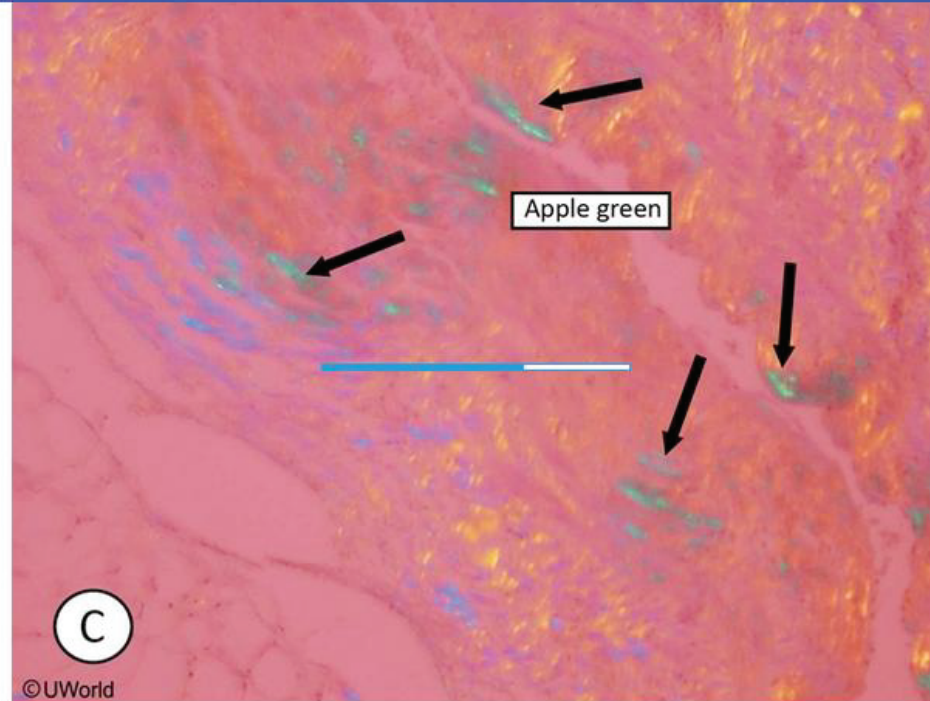


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dry eye symptoms are more consistent with Sjögren syndrome.

(Choice C) Pemphigus vulgaris is an autoimmune disease characterized by painful, flaccid bullae and erosions of the skin and mucosa. Biopsy of an active lesion will show intraepithelial cleavage with detached keratinocytes (acantholysis), retained keratinocytes along the basement membrane, and an eosinophilic inflammatory infiltrate.

(Choice E) Sarcoidosis is an inflammatory disease characterized by noncaseating granuloma formation in multiple tissues. Pulmonary and constitutional symptoms are common. Ocular involvement may cause uveitis, but conjunctival erythema and dry eye symptoms are more consistent with Sjögren syndrome.

Educational objective:

Sjögren syndrome is an autoimmune disorder characterized by inflammation of exocrine glands. Biopsy of the labial salivary glands shows periductal lymphocytic infiltrates (focal lymphocytic sialadenitis), often with germinal centers; the glandular tissue is typically atrophic and fibrotic.

References

- Salivary gland biopsy for Sjögren's syndrome.

Pathology

Rheumatology/Orthopedics & Sports

Sjogren syndrome





A 56-year-old man comes to the emergency department with acute onset of severe right foot pain. The pain is associated with local redness and swelling, but he has had no fever or recent trauma. The patient has never had similar symptoms. Medical history is significant for type 2 diabetes mellitus, mixed hyperlipidemia, hypertension, and coronary artery disease, for which he takes several medications. Physical examination shows a swollen, tender first metatarsophalangeal joint. Aspiration reveals a high leukocyte count, negative Gram stain, and numerous needle-shaped negatively birefringent crystals. Which of the following drugs is most likely to have precipitated this patient's condition?

- ☐ A. Atorvastatin
- ☐ B. Gemfibrozil
- ☐ C. Hydrochlorothiazide
- ☐ D. Losartan
- ☐ E. Metformin

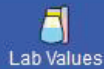
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A 56-year-old man comes to the emergency department with acute onset of severe right foot pain. The pain is associated with local redness and swelling, but he has had no fever or recent trauma. The patient has never had similar symptoms. Medical history is significant for type 2 diabetes mellitus, mixed hyperlipidemia, hypertension, and coronary artery disease, for which he takes several medications. Physical examination shows a swollen, tender first metatarsophalangeal joint. Aspiration reveals a high leukocyte count, negative Gram stain, and numerous needle-shaped negatively birefringent crystals. Which of the following drugs is most likely to have precipitated this patient's condition?

- ☐ A. Atorvastatin (2%)
- ☐ B. Gemfibrozil (9%)
- ☒ C. Hydrochlorothiazide (82%)
- ☐ D. Losartan (1%)
- ☐ E. Metformin (3%)





Risk factors for gout

| | |
|--|--|
| Increased uric acid production | <ul style="list-style-type: none">• Dietary sources<ul style="list-style-type: none">◦ Purine-rich foods (eg, seafood, red meat)◦ Fructose-containing & alcoholic beverages (particularly beer)• ↑ Cell turnover (eg, tumor lysis syndrome)• Lesch-Nyhan syndrome (deficiency of HGPRT)• ↑ Phosphoribosyl pyrophosphate activity |
| Decreased uric acid clearance | <ul style="list-style-type: none">• Chronic kidney disease• Volume depletion• Diuretics (eg, thiazide)• Cyclosporine & tacrolimus |
| Rapid decline in uric acid levels | <ul style="list-style-type: none">• Xanthine oxidase inhibitors (eg, allopurinol)• Uricosuric drugs (eg, probenecid) |

HGPRT = hypoxanthine-guanine phosphoribosyltransferase.





This patient has an acute inflammatory arthritis of the first metatarsophalangeal joint with needle-shaped, **negatively birefringent crystals** noted on joint fluid microscopy. This presentation is consistent with an acute **gout flare**, which occurs due to the deposition of monosodium urate crystals within joint spaces (most commonly in the lower extremities).

Gout occurs in the setting of **hyperuricemia**, which may occur due to increased uric acid production (eg, dietary sources of purine) or reduced uric acid clearance. Most **diuretics** (eg, hydrochlorothiazide, furosemide) can cause hyperuricemia and trigger gout flares by causing relative **volume depletion**, which decreases the fractional excretion of uric acid. Other medications that can cause hyperuricemia include certain immunosuppressants (eg, cyclosporine, tacrolimus) and cytotoxic chemotherapeutic agents. In addition, medications that rapidly lower uric acid levels (eg, allopurinol) can paradoxically trigger an acute attack of gout due to mobilization of tissue urate stores (ie, dissolving crystals become fragile and more easily shed into the joint space).

(Choices A and B) The lipid-lowering medication most prominently associated with gout is niacin, which decreases renal excretion of uric acid. Statins (eg, atorvastatin) can cause hepatitis and myalgias, and fibrates (eg, gemfibrozil, fenofibrate) can cause severe myopathy when given with statins; fibrates also increase the risk of cholesterol gallstones.





Item 22 of 40

Question Id: 167



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

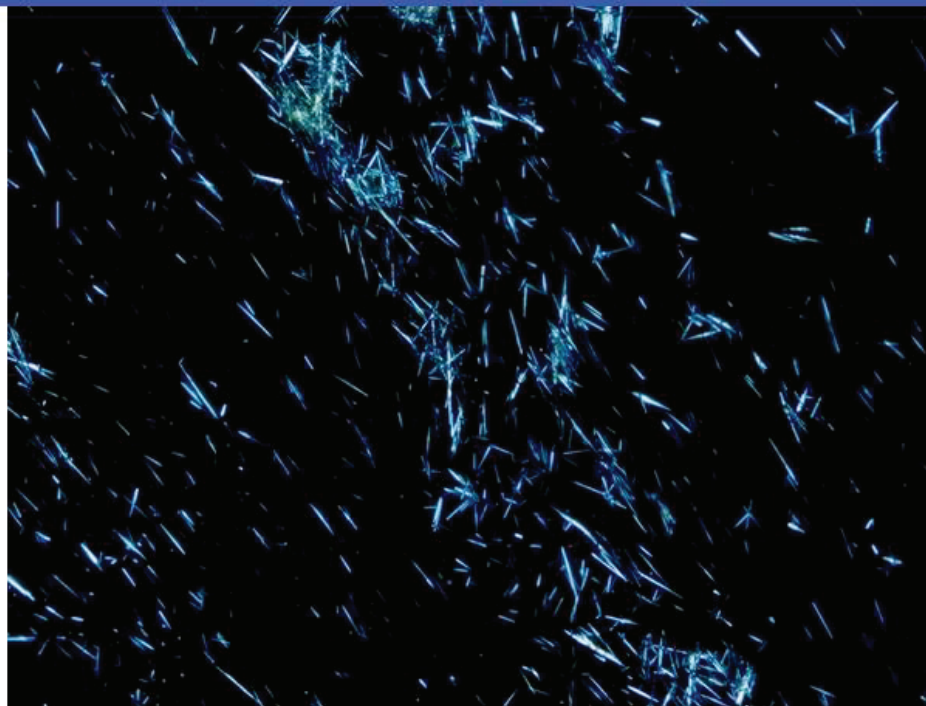


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Increase the risk of cholesterol gallstones.

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decreases renal excretion of uric acid. Statins (eg, atorvastatin) can cause hepatitis and myalgias, and fibrates (eg, gemfibrozil, fenofibrate) can cause severe myopathy when given with statins; fibrates also increase the risk of cholesterol gallstones.

(Choice D) Losartan has a mild uricosuric effect and can be used in hypertensive patients with gout without precipitating an acute attack of gout.

(Choice E) Metformin slightly lowers uric acid, possibly due to changes in fatty acid metabolism. It is not associated with a significant risk of gout.

Educational objective:

Gout occurs in the setting of hyperuricemia and causes an inflammatory arthritis characterized by negative birefringent, needle-shaped crystals visible on joint fluid microscopy. Most diuretics (eg, hydrochlorothiazide, furosemide) can cause hyperuricemia and trigger gout flares by causing relative volume depletion, which decreases the fractional excretion of uric acid.

Pharmacology

Rheumatology/Orthopedics & Sports

Gout

Subject

System

Topic

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A 64-year-old man comes to the emergency department due to acute knee pain. He developed redness, swelling, and severe pain affecting the right knee the day before his arrival. The patient has had 3 similar episodes in the past year that resolved quickly with over-the-counter analgesics. He has a history of polycythemia vera but has been noncompliant with phlebotomy treatments. Vital signs and cardiopulmonary examinations are normal. The right knee is red and warm. There is severe pain with movement at the joint; the other joints are grossly normal. Needle aspiration of the joint is performed. Which of the following is the most likely finding on analysis of this patient's synovial fluid?

- ☐ A. Clear fluid with few white blood cells
- ☐ B. Gram-negative diplococci
- ☐ C. Gram-positive cocci in clusters
- ☐ D. Many leukocytes with no crystals or organisms
- ☐ E. Needle-shaped, negatively birefringent crystals
- ☐ F. Numerous red blood cells
- ☐ G. Rhomboid-shaped, positively birefringent crystals





swelling, and severe pain affecting the right knee the day before his arrival. The patient has had 3 similar episodes in the past year that resolved quickly with over-the-counter analgesics. He has a history of polycythemia vera but has been noncompliant with phlebotomy treatments. Vital signs and cardiopulmonary examinations are normal. The right knee is red and warm. There is severe pain with movement at the joint; the other joints are grossly normal. Needle aspiration of the joint is performed. Which of the following is the most likely finding on analysis of this patient's synovial fluid?

- ☐ A. Clear fluid with few white blood cells (1%)
- ☐ B. Gram-negative diplococci (1%)
- ☐ C. Gram-positive cocci in clusters (3%)
- ☐ D. Many leukocytes with no crystals or organisms (6%)
- ☒ E. Needle-shaped, negatively birefringent crystals (56%)
- ☐ F. Numerous red blood cells (10%)
- ☐ G. Rhomboid-shaped, positively birefringent crystals (18%)





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Causes of gout

Increased urate production

- **Primary gout** (idiopathic)
- Myeloproliferative/lymphoproliferative disorders
- Tumor lysis syndrome
- Hypoxanthine guanine phosphoribosyl transferase deficiency

Decreased urate clearance

- Chronic kidney disease
- Thiazide/loop diuretics

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This patient, with recurrent acute monoarthritis and history of a myeloproliferative disorder, has typical features of **gout**. Gout occurs when there is an increased **uric acid** concentration in serum and synovial fluid, leading to monosodium urate crystal formation and deposition in synovium and cartilage. Gout is most common in joints where cooler temperatures favor crystal formation, especially in the distal lower extremity (eg, **first metatarsophalangeal joint**, ankle, knee). Uptake of urate crystals by neutrophils leads to free radical release, cytokine production, and joint inflammation. The hyperuricemia that predisposes to gout can be idiopathic (primary gout) or due to increased urate production (eg, myeloproliferative disorders) or decreased urate clearance by the kidneys.

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or decreased urate clearance by the kidneys.

Gouty arthritis presents with acute onset of severe joint pain, warmth, erythema, and swelling. The diagnosis is established by synovial fluid analysis, which shows increased white blood cells. **Monosodium urate crystals** are seen under polarized light microscopy and may be present both intra- and extracellularly. They are characteristically **needle-shaped** and **negatively birefringent** (when the crystals are aligned parallel to the slow ray of the compensator, they appear yellow; when aligned perpendicular, they appear blue).

(Choice A) Osteoarthritis causes chronic, progressive arthritis in the distal hands and weight-bearing joints. Synovial fluid analysis shows normal to minimal inflammatory findings.

(Choices B and C) Gonococcal arthritis presents with fever, skin lesions, and inflammatory mono- or oligoarthritis. Staphylococcal septic arthritis causes a fulminant monoarthritis, usually with fever. Recurrent episodes are more characteristic of gout.

(Choice D) Rheumatoid arthritis causes a chronic polyarthritis, typically involving the metacarpophalangeal joints of the hands. Synovial fluid will show a sterile inflammatory effusion.

(Choice F) Nontraumatic hemarthrosis is most commonly seen in patients taking anticoagulants (eg, warfarin) or with bleeding disorders (eg, hemophilia).





Item 23 of 40

Question Id: 1450



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



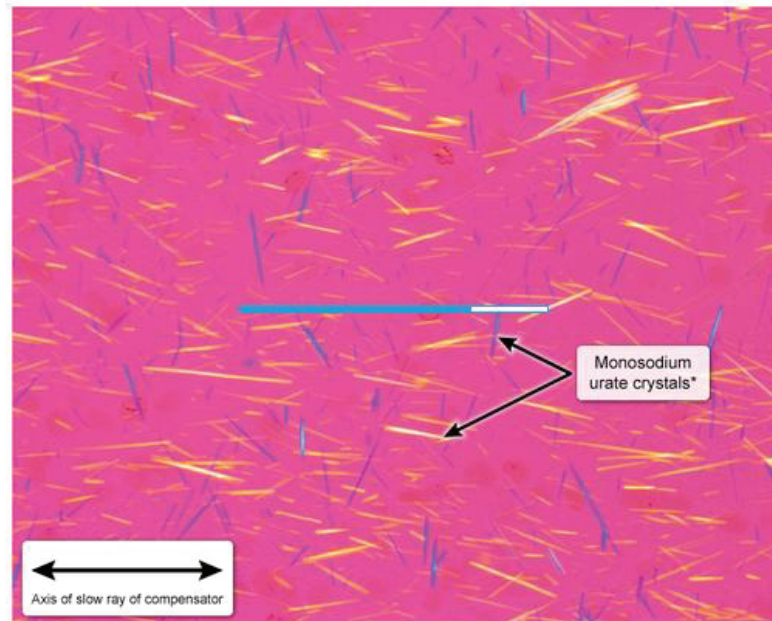
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Settings

Exhibit Display

Gout



*Needle-shaped, negatively birefringent crystals under compensated polarized light

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episodes are more characteristic of gout.

(Choice D) Rheumatoid arthritis causes a chronic polyarthritis, typically involving the metacarpophalangeal joints of the hands. Synovial fluid will show a sterile inflammatory effusion.

(Choice F) Nontraumatic hemarthrosis is most commonly seen in patients taking anticoagulants (eg, warfarin) or with bleeding disorders (eg, hemophilia).

(Choice G) Crystal arthritis due to calcium pyrophosphate deposition (pseudogout) most commonly affects the knee and is often similar to gout. However, it is less common and not associated with myeloproliferative disorders.

Educational objective:

Gout results from the deposition of monosodium urate crystals in the joints and soft tissues. Under polarized light, urate crystals appear needle-shaped and negatively birefringent. Conditions that increase uric acid production or decrease uric acid clearance can increase the risk of gout.

References

- [Hyperuricemia, gout, and related comorbidities: cause and effect on a two-way street.](#)

Pathophysiology Rheumatology/Orthopedics & Sports Gout

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A 3-year-old boy is brought to the emergency department for refusal to move his right arm. This afternoon, he tripped while holding hands with his sister, who pulled up on his arm to prevent him from falling. The patient immediately began to cry and has since refused to move the arm. On physical examination, he holds the right arm against his abdomen with the elbow flexed and forearm pronated. The patient cries with any attempted manipulation of the right elbow. There is no visible swelling or deformity. Which of the following structures is most likely affected in this patient's condition?

- ☐ A. Annular ligament
- ☐ B. Biceps tendon
- ☐ C. Interosseous membrane
- ☐ D. Radial collateral ligament
- ☐ E. Ulnar collateral ligament

Submit



A 3-year-old boy is brought to the emergency department for refusal to move his right arm. This afternoon, he tripped while holding hands with his sister, who pulled up on his arm to prevent him from falling. The patient immediately began to cry and has since refused to move the arm. On physical examination, he holds the right arm against his abdomen with the elbow flexed and forearm pronated. The patient cries with any attempted manipulation of the right elbow. There is no visible swelling or deformity. Which of the following structures is most likely affected in this patient's condition?

- ☒ A. Annular ligament (62%)
- ☐ B. Biceps tendon (8%)
- ☐ C. Interosseous membrane (2%)
- ☐ D. Radial collateral ligament (17%)
- ☐ E. Ulnar collateral ligament (8%)

Correct



62%

Answered correctly



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Time Spent



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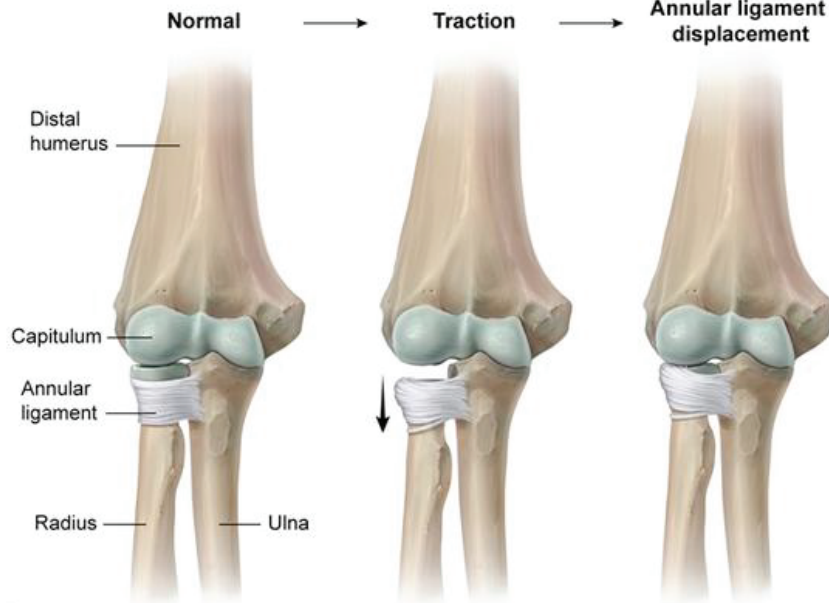
Normal

Traction

Annular ligament

Exhibit Display

Radial head subluxation (nursemaid's elbow)



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This patient's mechanism of injury (eg, sudden pulling up on the arm) and presentation (eg, holding the arm flexed and pronated, pain with movement) are consistent with **radial head subluxation** (ie, nursemaid's elbow).

The radial head is anchored to the ulna by the **annular ligament**, which encircles the proximal radius. In children age <5, this tissue is relatively thin compared to older children and adults. Sudden **axial traction** (eg, pulling up on the arm by the hand) or twisting can cause the annular ligament to slip over the radial head and become **entrapped** in the radiohumeral joint.

Patients classically hold the affected arm close to the body with the **elbow flexed** and the **forearm pronated**. There is significant pain with movement or manipulation of the joint but typically no obvious swelling or deformity. **Reduction** can usually be accomplished either by hyperpronation of the forearm or supination of the forearm with flexion of the elbow.

(Choice B) A distal biceps tendon rupture characteristically occurs in older patients after forceful extension of the elbow while the biceps muscle is contracted, resulting in a visible mass in the mid-upper arm (ie, "Popeye" deformity).

(Choice C) The interosseous membrane is a broad sheet of connective tissue between the radius and





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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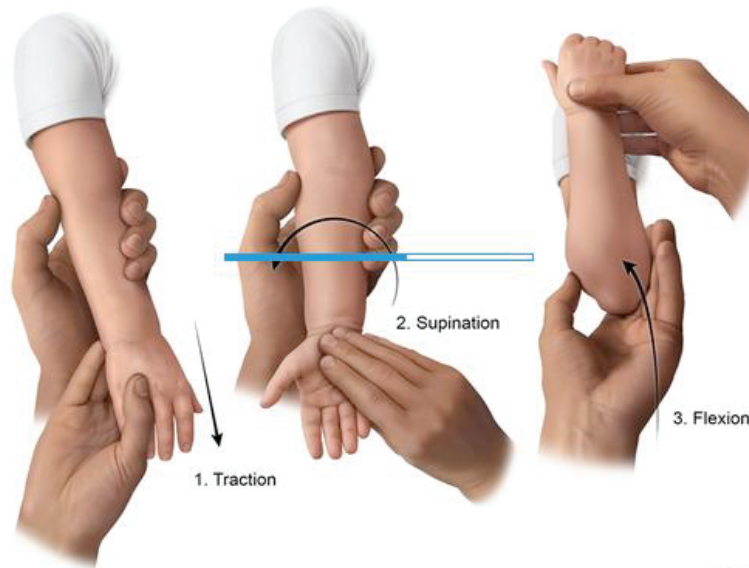


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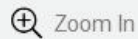
Exhibit Display

Nursemaid's elbow reduction maneuvers Nursemaid's elbow reduction maneuvers

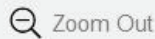
Supination & flexion



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(Choice C) The interosseous membrane is a broad sheet of connective tissue between the radius and

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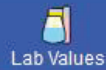
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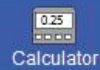
Tutorial



Lab Values



Notes



Calculator



Reverse Color



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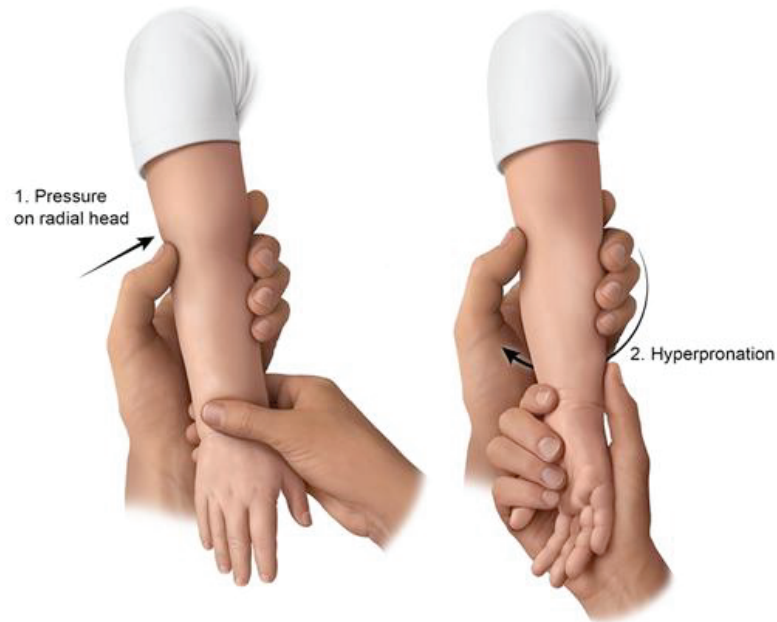


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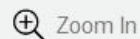
Exhibit Display

Nursemaid's elbow reduction maneuvers [Nursemaid's elbow reduction maneuvers](#)

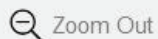
Extension & hyperpronation



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Zoom In



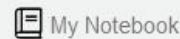
Zoom Out



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Block time remaining: 00:28:49

TUTOR

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Feedback



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of the elbow while the biceps muscle is contracted, resulting in a visible mass in the mid-upper arm (ie, "Popeye" deformity).

(Choice C) The interosseous membrane is a broad sheet of connective tissue between the radius and ulna that provides forearm stability and a point of attachment for the forearm muscles. Injury to the membrane is associated with fracture of the radius or ulna after a fall onto an outstretched hand.

(Choice D) Injury to the radial (lateral) collateral ligament of the elbow can occur with acute varus stress during a fall onto an outstretched hand and is often associated with fracture or dislocation of the elbow.

(Choice E) The ulnar (medial) collateral ligament is typically injured by intense, repetitive overuse involving a valgus stress at the elbow (eg, pitching a baseball), resulting in medial elbow pain that increases during throwing motions.

Educational objective:

Radial head subluxation (ie, nursemaid's elbow) is the displacement of the annular ligament into the radiohumeral joint, classically resulting from sudden axial traction (eg, pulling) on the arm of a child age <5. Although most patients do not have any obvious swelling or deformity, they avoid moving the arm due to pain and hold it with the elbow flexed and forearm pronated.

References





A 27-year-old man comes to the emergency department with progressive right knee swelling and pain. He has no history of trauma to the area. The patient has no other medical conditions and takes no medications. X-rays reveal a large lytic lesion involving the proximal tibia with extensive soft-tissue swelling. After additional confirmatory testing, the patient undergoes a right-sided, above-knee amputation. Histologic examination of the resected mass is shown in the [exhibits](#). Which of the following is the most likely diagnosis?

- ☐ A. Chondrosarcoma
- ☐ B. Ewing sarcoma
- ☐ C. Metastatic adenocarcinoma
- ☐ D. Osteoid osteoma
- ☐ E. Osteosarcoma

Submit





Item 25 of 40

Question Id: 15636



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



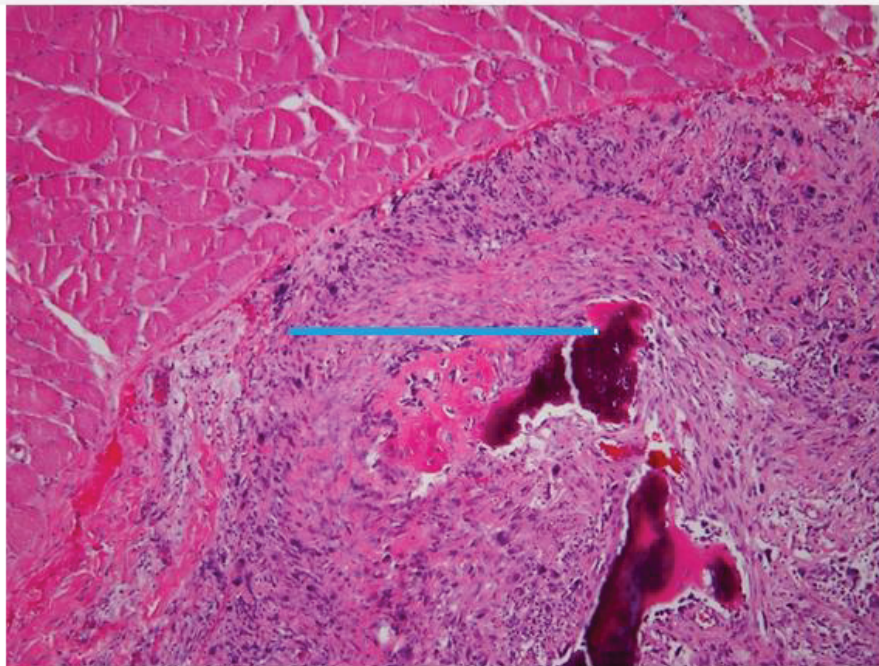
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Exhibit 1 Exhibit 2



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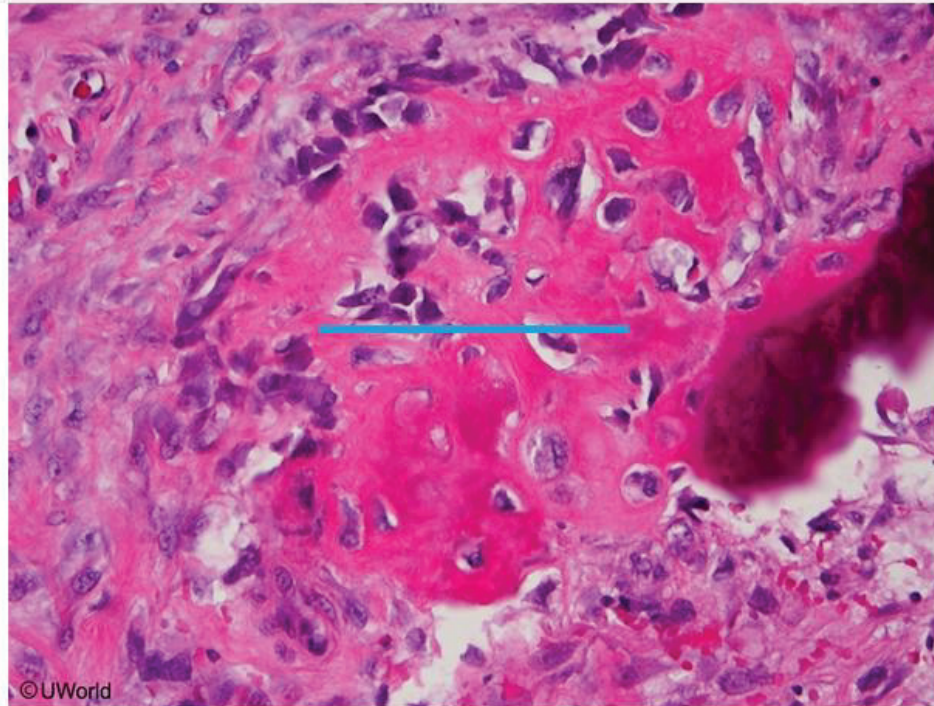
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End Block

Exhibit Display

Exhibit 1 Exhibit 2



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A 27-year-old man comes to the emergency department with progressive right knee swelling and pain. He has no history of trauma to the area. The patient has no other medical conditions and takes no medications. X-rays reveal a large lytic lesion involving the proximal tibia with extensive soft-tissue swelling. After additional confirmatory testing, the patient undergoes a right-sided, above-knee amputation. Histologic examination of the resected mass is shown in the exhibits. Which of the following is the most likely diagnosis?

- ☐ A. Chondrosarcoma (23%)
- ☐ B. Ewing sarcoma (13%)
- ☐ C. Metastatic adenocarcinoma (1%)
- ☐ D. Osteoid osteoma (6%)
- ☒ E. Osteosarcoma (55%)

Correct

55%
Answered correctly

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Previous



Next



Full Screen



Tutorial



Lab Values



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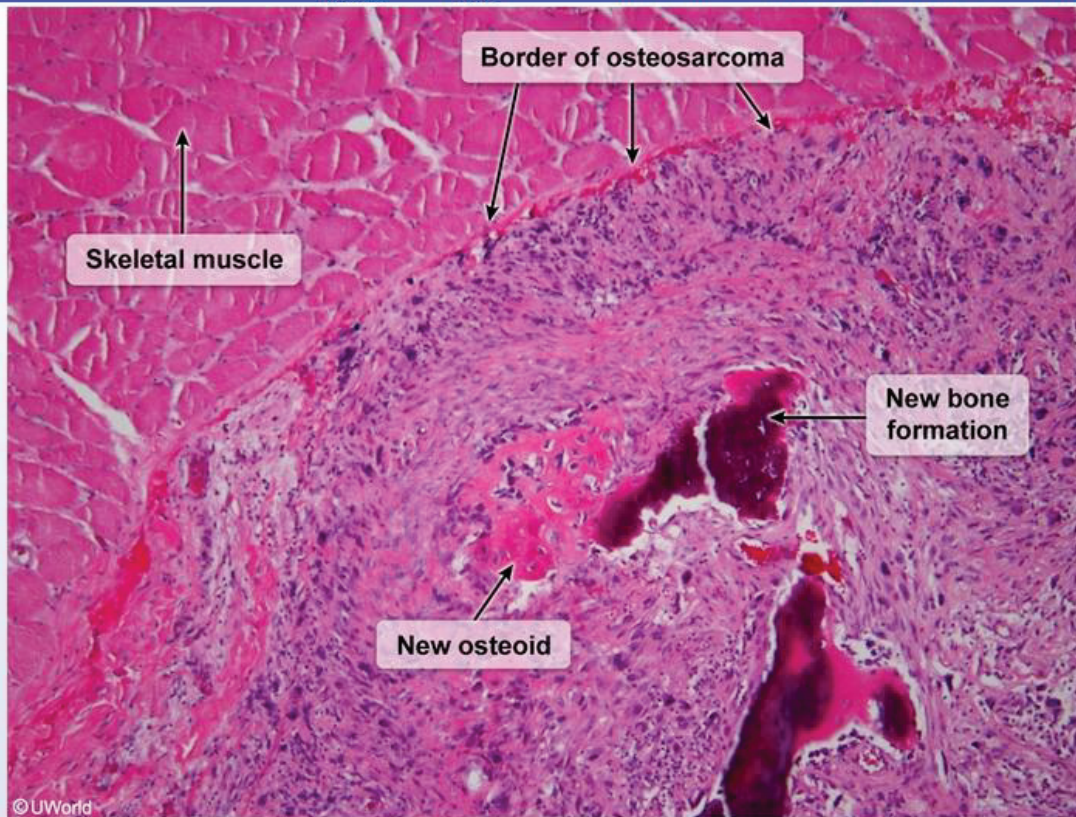
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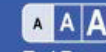
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This patient's spindle-shaped tumor cells admixed with bone and osteoid indicates **osteosarcoma**, the most common primary bone tumor in children and young adults. Most cases arise in the **metaphyses of long bones** (eg, proximal tibia), the location of the growth plate and site of greatest bone proliferation. Patients typically present with **pain and soft-tissue swelling**, and x-ray usually reveals a **lytic bone lesion**.

Osteosarcomas arise from a malignant mesenchymal stem cell that generates cartilage, bone, or fibrous tissue. Therefore, the diagnosis is confirmed when histopathology reveals neoplastic **spindle-shaped stromal cells** admixed with **tumor osteoid** and thin trabeculae of bone.

(Choice A) Unlike osteosarcomas, chondrosarcomas and fibrosarcomas do not produce osteoid or bone. **Chondrosarcomas** are characterized by neoplastic chondrocytes in a hyaline cartilage matrix, usually with small calcifications.

(Choice B) Ewing sarcoma, the second most common primary bone malignancy in young patients, often arises in long bones and causes progressive pain, swelling, and lytic bone lesions. However, histopathology reveals sheets of **small, round, cells** separated by fibrous septae and patches of necrosis/hemorrhage; no osteoid or bone is produced.

(Choice C) Adenocarcinoma of the lung often metastasizes to bone. However, histology would show **neoplastic glands** lined with mucin-producing cells.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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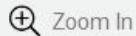
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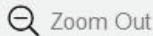
Osteosarcoma



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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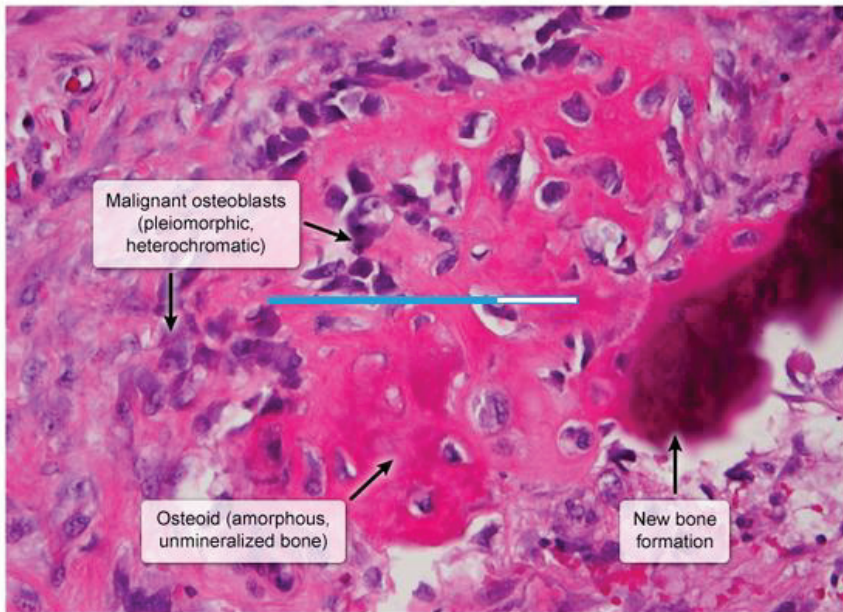
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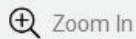
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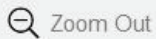
Osteosarcoma



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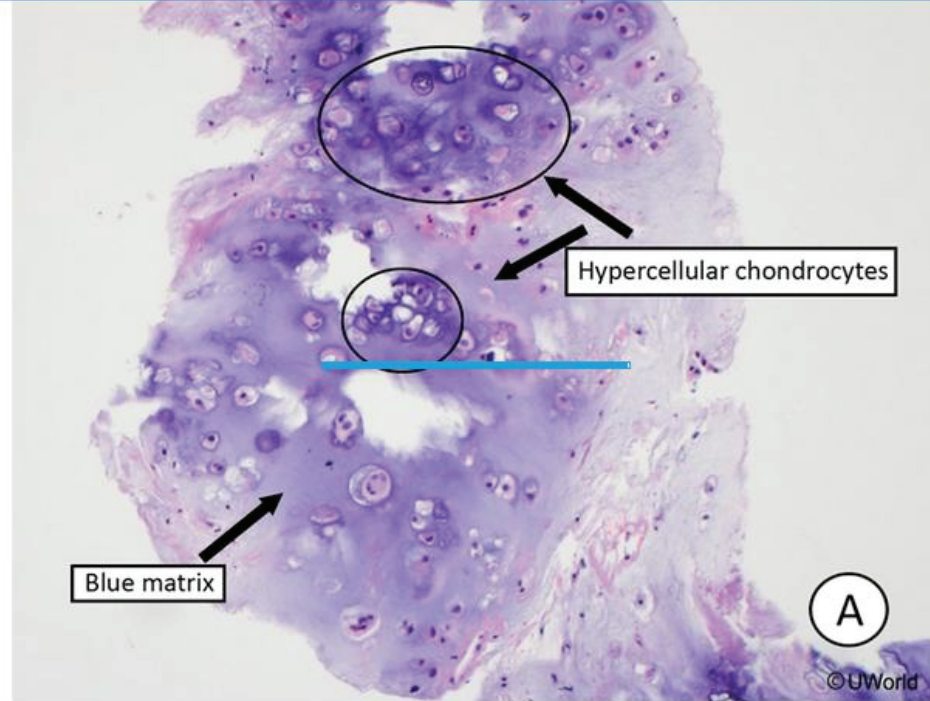


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Exhibit Display



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Intestine is lined with mucin-producing cells



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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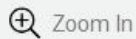
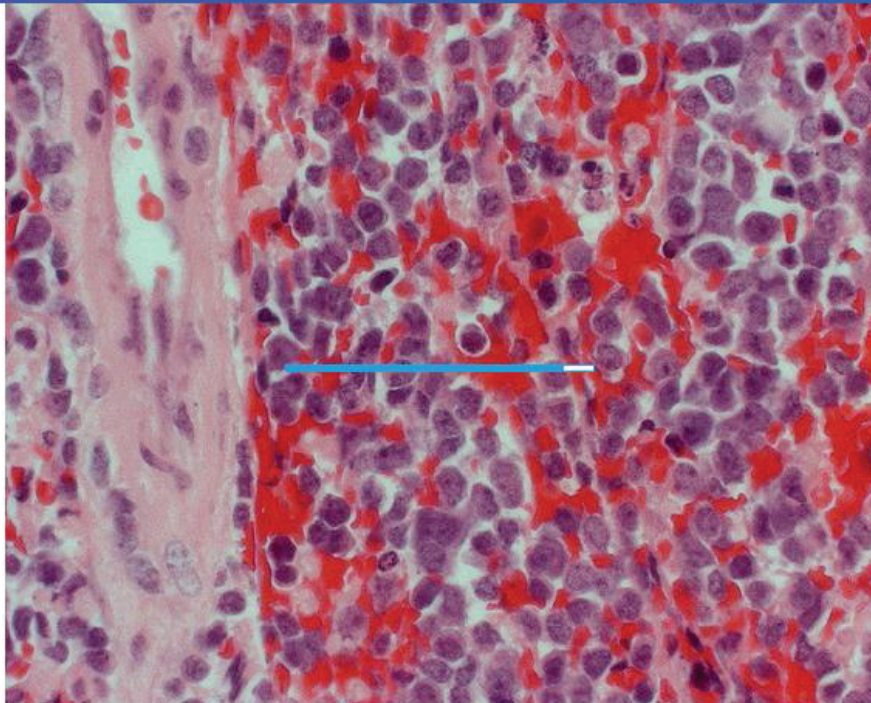


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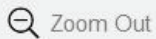


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Intestine is lined with mucin-producing cells

Block Time Remaining: 00:29:43

TUTOR

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Feedback



Suspend



End Block



necrosis/hemorrhage; no osteoid or bone is produced.

(Choice C) Adenocarcinoma of the lung often metastasizes to bone. However, histology would show **neoplastic glands** lined with mucin-producing cells.

(Choice D) Osteoid osteoma is a small, benign, bone-forming tumor that typically occurs in adolescent boys. Histopathology shows irregular patterns of woven bone lined by a single layer of benign-appearing osteoblasts. The presence of a large lytic bone lesion and highly pleomorphic spindle-shaped tumor cells makes this diagnosis unlikely.

Educational objective:

Osteosarcoma is the most common primary bone tumor in children and young adults and typically arises near the metaphyses of long bones. Patients usually have slowly worsening pain and soft-tissue swelling. X-ray typically reveals a lytic bone lesion, and biopsy classically shows pleomorphic, spindle-shaped tumor cells that generate osteoid and thin trabeculae of neoplastic bone.

References

- [Osteosarcoma](#).

Pathology

Rheumatology/Orthopedics & Sports

Bone tumor





Item 25 of 40

Question Id: 15636



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



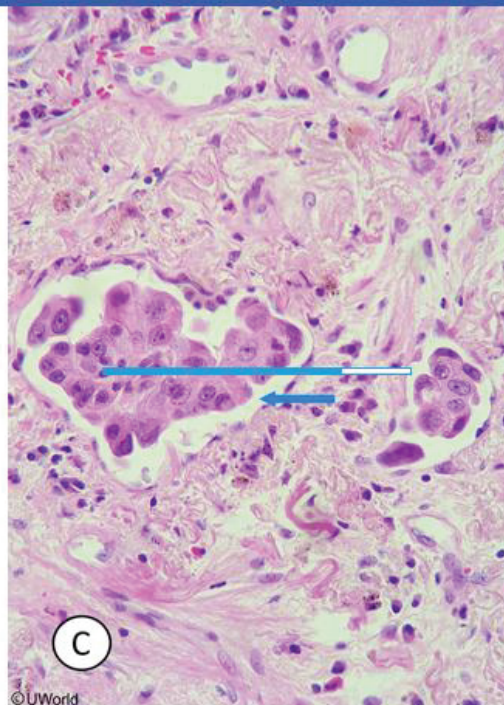
Text Zoom



Settings

necrosis/hemorrhage: no osteoid or bone is produced

Exhibit Display



Zoom In

Zoom Out

Reset

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My Notebook

Block Time Remaining: 00:29:43

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<https://t.me/USMLEWorldStep1>



1



Feedback



Suspend



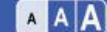
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A 60-year-old man comes to the office due to a 4-month history of increasing midthoracic back pain, which is aggravated by coughing. The patient has also had right thigh pain but no numbness or weakness in the legs and no bowel or bladder incontinence. He has no other medical conditions. Vital signs are within normal limits. On examination, there is tenderness over the eighth and ninth thoracic vertebrae. Neurologic examination is normal. The prostate is normal in size and has no palpable nodules. Imaging studies reveal enlarged vertebral bodies with cortical thickening. Serum testing for which of the following would most likely help establish a diagnosis in this patient?

- ☐ A. 25-hydroxyvitamin D level
- ☐ B. Alkaline phosphatase level
- ☐ C. Erythrocyte sedimentation rate
- ☐ D. Parathyroid hormone level
- ☐ E. Prostate-specific antigen level

Submit



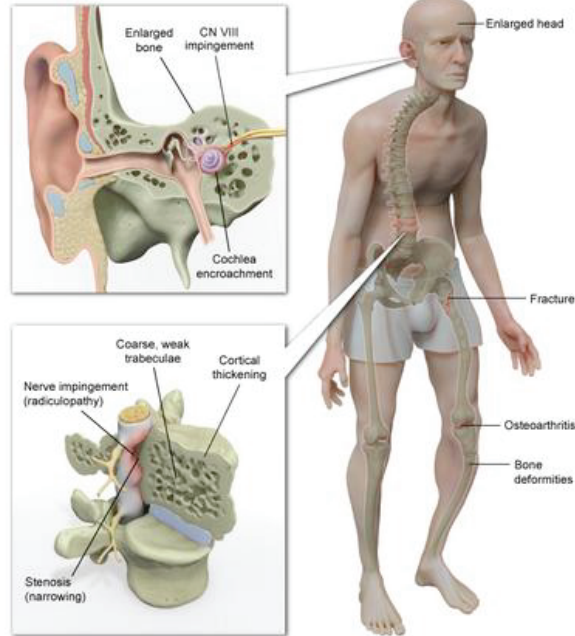
A 60-year-old man comes to the office due to a 4-month history of increasing **midthoracic back pain**, which is aggravated by **coughing**. The patient has also had **right thigh pain** but no numbness or weakness in the legs and no bowel or bladder incontinence. He has no other medical conditions. Vital signs are within normal limits. On examination, there is tenderness over the eighth and ninth thoracic vertebrae. Neurologic examination is normal. The prostate is normal in size and has no palpable nodules. Imaging studies reveal **enlarged vertebral bodies** with **cortical thickening**. Serum testing for which of the following would most likely help establish a diagnosis in this patient?

- ☐ A. 25-hydroxyvitamin D level (4%)
- ☒ B. Alkaline phosphatase level (75%)
- ☐ C. Erythrocyte sedimentation rate (4%)
- ☐ D. Parathyroid hormone level (8%)
- ☐ E. Prostate-specific antigen level (7%)



Exhibit Display

Clinical features of Paget disease of bone



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This older patient with multifocal bone pain has enlarged vertebral bodies with cortical thickening on imaging, which is consistent with **Paget disease of bone (PD)**. PD is characterized by **excessive and disordered bone formation**. It commonly affects the skull, long bones of the extremities, and vertebral column. In addition to pain and deformity, vertebral involvement can lead to spinal stenosis, nerve compression, and compression fracture.

The increased formation of new bone in PD is associated with an **elevated serum alkaline phosphatase** level, but because the changes occur slowly, serum calcium and phosphorus levels are often normal.

Radiographs typically reveal lytic or mixed lytic-sclerotic lesions, **thickening of cortical and trabecular bone**, and bony deformities. In the vertebrae, bony enlargement and cortical thickening may create an appearance resembling a **picture frame**.

(Choice A) The level of 25-hydroxyvitamin D reflects total body vitamin D stores and is useful in the diagnosis of osteomalacia. In addition to bone pain, osteomalacia causes muscle weakness and difficulty walking. X-ray reveals diffuse demineralization, often with insufficiency fractures, rather than cortical thickening.

(Choice C) The erythrocyte sedimentation rate reflects circulating levels of inflammatory proteins and is elevated in many inflammatory and malignant conditions. It is classically elevated in polymyalgia



elevated in many inflammatory and malignant conditions. It is classically elevated in polymyalgia rheumatica; this condition causes pain in the shoulders, hips, and proximal extremities, but x-rays are normal. It can also be strikingly elevated in multiple myeloma, which can cause osteolytic lesions resembling early pagetic lesions but does not cause cortical thickening.

(Choice D) Hyperparathyroidism can present with bone pain, typically in association with hypercalcemic manifestations (eg, constipation, renal stones). X-ray of the vertebral column reveals cortical thinning, not thickening.

(Choice E) Prostate-specific antigen is used in the diagnosis of prostate cancer. Bone metastasis in prostate cancer appears on x-ray as focal sclerotic lesions, and most patients have palpable nodules on prostate examination.

Educational objective:

Paget disease of bone is characterized by excessive and disordered bone formation. It commonly affects the skull, long bones, and vertebral column. The increased formation of new bone is associated with an elevated serum alkaline phosphatase level. Radiographs shows lytic or mixed lytic-sclerotic lesions, thickening of cortical and trabecular bone, and bony deformities.

Pathology Rheumatology/Orthopedics & Sports Pagets disease of bone

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End Block



A 42-year-old weightlifter is preparing for an upcoming strength competition. After lifting a series of progressively heavier weights, he decides to increase the weight on the exercise bar to 175 kg (385 lbs), the heaviest lift he has ever attempted. He is able to hold the weight over his head for several seconds. However, his arms suddenly and involuntarily give way and he drops the weight to the ground. Which of the following structures was most likely responsible for the sudden muscle relaxation?

- ☐ A. A-delta nerve endings
- ☐ B. Golgi tendon organ
- ☐ C. Intrafusal muscle fibers
- ☐ D. Pacinian corpuscles
- ☐ E. Ruffini's end organs

Submit

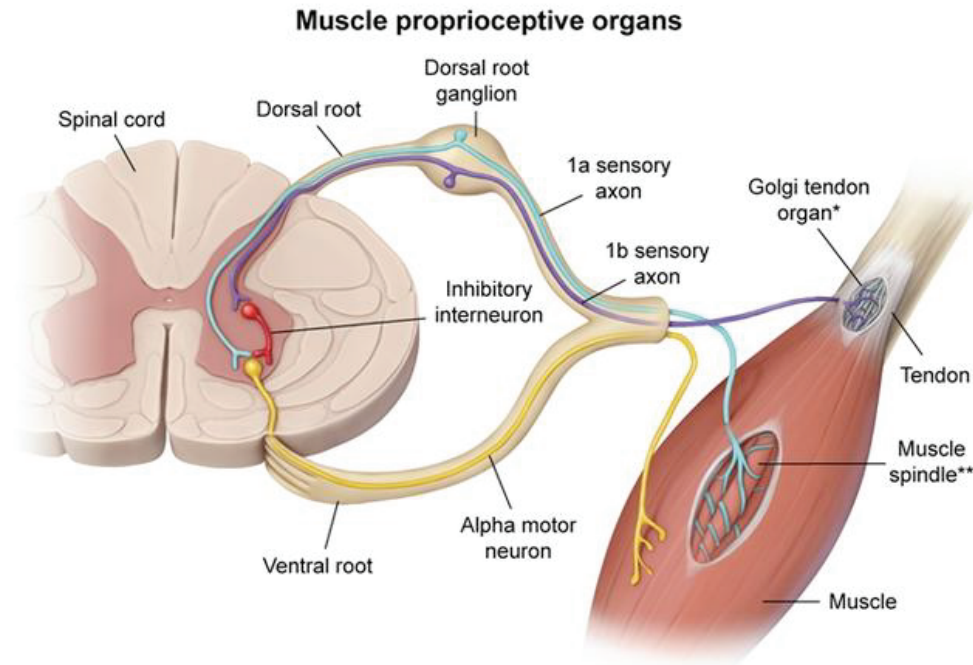


A 42-year-old weightlifter has been progressively increasing the weight of the heaviest lift he performs over the past 6 months. However, his arm has become increasingly numb and tingling over the following 3 months.

- ☐ A. A-delta fibers
- ☒ B. Golgi tendon organs
- ☐ C. Intrafusal fibers
- ☐ D. Pacinian corpuscles
- ☐ E. Ruffini endings

Submit

Exhibit Display



*Detects changes in muscle tension & inhibits muscle contraction, preventing damage
**Detects changes in muscle length & activates muscle contraction (reflex testing)

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A 42-year-old weightlifter is preparing for an upcoming strength competition. After lifting a series of progressively heavier weights, he decides to **increase** the weight on the exercise bar to 175 kg (385 lbs), the heaviest lift he has ever attempted. He is able to hold the weight over his head for several seconds. However, his arms **suddenly** and involuntarily give way and he drops the weight to the ground. Which of the following structures was most likely responsible for the sudden muscle relaxation?

- ☐ A. A-delta nerve endings (4%)
- ☒ B. Golgi tendon organ (71%)
- ☐ C. Intrafusal muscle fibers (18%)
- ☐ D. Pacinian corpuscles (3%)
- ☐ E. Ruffini's end organs (1%)

Correct



71%

Answered correctly



01 min, 27 secs

Time Spent



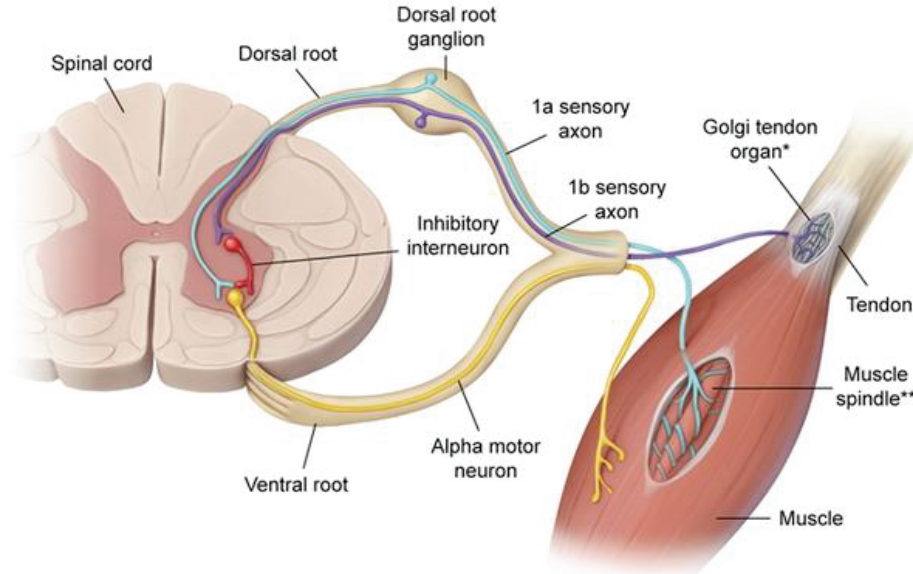
12/21/2020

Last Updated



Exhibit Display

Muscle proprioceptive organs



*Detects changes in muscle tension & inhibits muscle contraction, preventing damage

**Detects changes in muscle length & activates muscle contraction (reflex testing)

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My Notebook



*Detects changes in muscle tension & inhibits muscle contraction, preventing damage

**Detects changes in muscle length & activates muscle contraction (reflex testing)

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The Golgi tendon organs (GTOs) are sensory receptors located at the junction of the muscle and tendon that are innervated by group Ib sensory axons. GTOs are connected in series with the contracting extrafusal skeletal muscle fibers. When a muscle actively contracts against resistance, the increase in tension is transmitted through the tendon activating the GTOs in the process. In contrast, GTOs are relatively insensitive to changes in muscle length because the lengthening that occurs when a muscle is passively stretched takes place primarily in the muscle fibers and not in the tendon.

The Ib sensory axons from the GTOs contact inhibitory interneurons in the spinal cord, which in turn synapse with the α motor neurons that innervate the same muscle. Thus, the Golgi tendon circuit is a negative feedback system that regulates and maintains muscle tension. When a muscle exerts too much force, the GTOs inhibit contraction of the muscle, causing sudden muscle relaxation. This prevents damage to the musculoskeletal system.

(Choice A) A-delta fibers are thin, myelinated nerve fibers whose free nerve endings detect temperature and nociceptive stimuli. They are associated with acute (sharp) pain and constitute the afferent portion of the reflex arc that mediates withdrawal from noxious stimuli (e.g., retracting the hand away from a hot stove).



(Choice C) In contrast to the in-series arrangement of GTOs, muscle spindles (intrafusal muscle fibers) are connected in parallel with extrafusal fibers. They are innervated by group Ia and group II sensory axons and are sensitive to changes in muscle length. Muscle spindles mediate the stretch reflex (myotatic reflex), which is commonly tested (deep tendon reflexes) during the neurologic examination. When a muscle is stretched, there is monosynaptic reflex activation of the α motor neuron (of the same muscle), causing contraction that resists the stretch.

(Choices D and E) Pacinian corpuscles are *rapidly* adapting mechanoreceptors located in the subcutaneous tissue of the skin as well as the mesentery, peritoneum, and joint capsules. Ruffini's end organs are *slowly* adapting mechanoreceptors that exist in the skin, subcutaneous tissue, and joint capsule. Both help to mediate touch, proprioception, and vibratory sensation and are innervated by myelinated A-beta fibers.

Educational objective:

The muscle spindle system is a feedback system that monitors and maintains muscle length, while the Golgi tendon system is a feedback system that monitors and maintains muscle force. GTOs are exquisitely sensitive to increases in muscle tension but are relatively insensitive to passive stretch.

References



A 45-year-old Caucasian female suffers from recurrent nonpitting edema of the hands. She often wears warm gloves indoors because her fingers turn blue when they are cold. She also complains of retrosternal burning and regurgitation, especially when supine. Which of the following antibodies is most likely to be found in this patient?

- ☐ A. Anti-dsDNA
- ☐ B. Anti-centromere
- ☐ C. Anti-histone
- ☐ D. Anti-SSA and SSB
- ☐ E. Anti-phospholipid

Submit



A 45-year-old Caucasian female suffers from recurrent nonpitting edema of the hands. She often wears warm gloves indoors because her fingers turn blue when they are cold. She also complains of retrosternal burning and regurgitation, especially when supine. Which of the following antibodies is most likely to be found in this patient?

- ☐ A. Anti-dsDNA (6%)
- ☒ B. Anti-centromere (77%)
- ☐ C. Anti-histone (2%)
- ☐ D. Anti-SSA and SSB (9%)
- ☐ E. Anti-phospholipid (3%)

Correct



77%

Answered correctly



01 min, 04 secs

Time Spent



01/30/2021

Last Updated





There are two main subtypes of systemic sclerosis: diffuse scleroderma, which is characterized by diffuse skin and visceral involvement, and CREST syndrome, which is associated with localized skin involvement and a more benign course. "CREST" is an acronym for the signs and symptoms: **C**alcinosis, **R**aynaud's phenomenon, **E**sophageal dysmotility, **S**clerodactyly and **T**elangiectasias. Anti-centromere antibodies are specific for CREST syndrome and found in 40% of cases. Anti-DNA topoisomerase I (Scl-70) antibodies are highly specific for systemic sclerosis (diffuse scleroderma).

The patient in the vignette has CREST syndrome. **Raynaud's phenomenon** causes painful episodes of pallor, cyanosis, and erythema of the hands in response to cold or emotional stress. These episodes of vasospasm can last minutes to hours. **Esophageal dysmotility** is the result of fibrosis of the distal esophagus with associated esophageal hypomotility. It manifests with symptoms of gastroesophageal reflux (heartburn and regurgitation). **Sclerodactyly** is thickening of the skin of the hands and feet. It begins as non-pitting edema of the hands and fingers. Later in the course of the disease, the skin becomes thickened, tight and shiny. Thinning of the skin (atrophy) follows. **Telangiectasias** (dilated blood vessels) occur on the skin of the face, hands and upper trunk, and on mucosal surfaces. **Calcinosis** refers to subcutaneous calcium deposits which may be asymptomatic or painful.

(Choice A) Anti-dsDNA antibodies are specific for systemic lupus erythematosus (SLE). Patients with SLE



(Choice A) Anti-dsDNA antibodies are specific for systemic lupus erythematosus (SLE). Patients with SLE commonly have a malar ("butterfly") facial rash that worsens with sun exposure. Patients also complain of low-grade fever, joint swelling and/or tenderness, and oral ulcers.

(Choice C) Anti-histone antibodies are found in drug-induced lupus. Procainamide, hydralazine, isoniazid, and D-penicillamine are common causes of drug-induced lupus. Symptoms resemble those of SLE, but without renal or CNS involvement.

(Choice D) Anti-Ro/SSA and anti-La/SSB antibodies are found in patients with Sjogren syndrome. This condition is characterized by keratoconjunctivitis sicca (dry eyes) and xerostomia (dry mouth). There may also be parotid gland enlargement, increased risk of other autoimmune diseases, and increased risk of non-Hodgkin lymphomas.

(Choice E) Anti-phospholipid antibodies are found in patients with SLE and in antiphospholipid antibody syndrome. Antiphospholipid antibody syndrome causes a hypercoagulable state and patients may suffer recurrent miscarriages. Partial thromboplastin time (PTT) is paradoxically increased in these patients despite the propensity toward thrombosis.

Educational Objective:

CREST syndrome (limited scleroderma) manifests with calcinosis, Raynaud's phenomenon, esophageal

(Choice D) Anti-Ro/SSA and anti-La/SSB antibodies are found in patients with Sjogren syndrome. This condition is characterized by keratoconjunctivitis sicca (dry eyes) and xerostomia (dry mouth). There may also be parotid gland enlargement, increased risk of other autoimmune diseases, and increased risk of non-Hodgkin lymphomas.

(Choice E) Anti-phospholipid antibodies are found in patients with SLE and in antiphospholipid antibody syndrome. Antiphospholipid antibody syndrome causes a hypercoagulable state and patients may suffer recurrent miscarriages. Partial thromboplastin time (PTT) is paradoxically increased in these patients despite the propensity toward thrombosis.

Educational Objective:

CREST syndrome (limited scleroderma) manifests with calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasias. Anti-centromere antibodies are found in about 40% of patients with CREST syndrome. Anti-DNA topoisomerase I (Scl-70) antibodies are highly specific for systemic sclerosis.

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|-----------|-----------------------------------|--------------------|
| Pathology | Rheumatology/Orthopedics & Sports | Systemic sclerosis |
| Subject | System | Topic |



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Previous



Next



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Tutorial



Lab Values



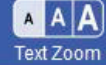
Notes



Calculator



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Text Zoom



Settings

A 62-year-old woman comes to the office due to a 3-month history of progressive muscle weakness. The patient has been having difficulty with activities such as getting out of the car and carrying groceries from the store. She has also developed a rash on her face and hands. The patient has a history of well-controlled hypertension and does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows weakness of shoulder abduction and hip flexion. Strength of the distal limb muscles and deep tendon reflexes are normal. Skin examination findings are shown in the [exhibit](#). Which of the following is the most appropriate initial treatment for this patient's current condition?

- ☐ A. Acetylcholinesterase inhibitors
- ☐ B. Copper supplementation
- ☐ C. Riluzole therapy
- ☒ D. Systemic glucocorticoids
- ☐ E. Thyroid hormone replacement

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Feedback



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Lab Values



Notes



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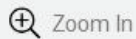


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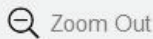


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Exhibit Display



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Previous



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Tutorial



Lab Values



Notes



Calculator



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Settings

A 62-year-old woman comes to the office due to a 3-month history of progressive muscle weakness. The patient has been having difficulty with activities such as getting out of the car and carrying groceries from the store. She has also developed a rash on her face and hands. The patient has a history of well-controlled hypertension and does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows weakness of shoulder abduction and hip flexion. Strength of the distal limb muscles and deep tendon reflexes are normal. Skin examination findings are shown in the exhibit. Which of the following is the most appropriate initial treatment for this patient's current condition?

- ☐ A. Acetylcholinesterase inhibitors (3%)
- ☐ B. Copper supplementation (0%)
- ☐ C. Riluzole therapy (2%)
- ☒ D. Systemic glucocorticoids (92%)
- ☐ E. Thyroid hormone replacement (0%)



0



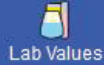
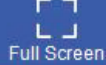
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Dermatomyositis is an autoimmune disorder characterized by:

- **Cutaneous manifestations: Gottron papules** (red or violaceous, flat-topped papules over joints and bony prominences, especially on the hands) and **heliotrope rash** (erythematous or violaceous edematous eruption on the upper eyelids and periorbital skin)
- **Myopathy:** Proximal muscle weakness (similar to polymyositis), elevated muscle enzymes (eg, creatine kinase, aldolase)

Autoantibodies, including antinuclear antibodies (more sensitive) and **anti-Jo-1** antibodies (more specific), are frequently positive. Muscle biopsy confirms the diagnosis and shows **perifascicular** inflammation and atrophy affecting a contiguous portion of the fascicle and surrounding blood vessels.

Initial treatment includes **systemic glucocorticoids** (eg, prednisone). Dermatomyositis may occur alone or as a paraneoplastic syndrome associated with **malignancy** (especially adenocarcinoma); affected patients should be evaluated for an underlying occult malignancy.

(Choice A) Acetylcholinesterase inhibitors (eg, physostigmine) are used in treatment of myasthenia gravis, which presents with fluctuating and fatigable weakness that primarily involves the ocular, bulbar, and respiratory muscles. The skin is not typically involved.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

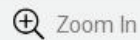
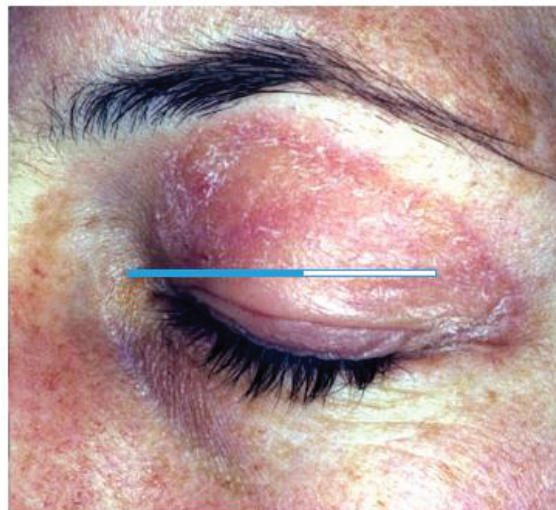


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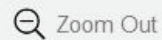


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Exhibit Display



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Feedback



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End Block



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



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Text Zoom



Settings

respiratory muscles. The skin is not typically involved.

(Choice B) Copper deficiency typically presents with muscle weakness, anemia, and fragile (kinky) hair.

Skin hypopigmentation is also common, but rash does not occur.

(Choice C) Riluzole is a glutamate inhibitor that is indicated for amyotrophic lateral sclerosis, a progressive neurodegenerative disorder that affects both upper and lower motor nerves. Although proximal muscle weakness may be seen (lower motor neuron dysfunction), upper motor neuron signs (eg, bulbar dysfunction, hyperreflexia) are expected and the disease is not associated with skin rash.

(Choice E) Hypothyroid myopathy commonly presents with proximal muscle weakness. However, unlike polymyositis and dermatomyositis, patients usually also have prominent muscle pain and often have other hypothyroid features (eg, weight gain, cold intolerance).

Educational objective:

Dermatomyositis is characterized by proximal muscle weakness (similar to polymyositis) and dermal manifestations (eg, heliotrope rash, Gottron papules). Laboratory testing shows elevated muscle enzymes (eg, creatine kinase) and autoantibodies (eg, antinuclear, anti-Jo-1). Initial treatment includes systemic glucocorticoids and evaluation for potential underlying malignancy.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 20-year-old man comes to the office due to pain in the left thigh. Three months ago, a horse kicked him in the left midthigh, resulting in deep pain and swelling in the thigh muscles; x-ray was normal, and, over the next several days, the symptoms resolved with rest and ice packs. However, a few weeks later, the patient gradually developed recurrent pain and swelling in the same area. Vital signs are normal. Examination shows a solitary, hard, mobile, oval mass of approximately 4 × 5 cm in the anterior aspect of the left thigh. Excision of the mass is performed. Histologic examination is likely to show which of the following?

- ☐ A. Benign metaplastic bone with surrounding fibroblastic proliferation
- ☐ B. Closely packed, small, round, uniform neoplastic cells
- ☐ C. Mature adipocytes with focal large, atypical hyperchromatic cells
- ☐ D. Pleomorphic neoplastic spindle cells producing new woven bone
- ☐ E. Synovial cyst filled with gelatinous mucoid material

Submit

Block Time Remaining: 00:34:48

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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 20-year-old man comes to the office due to pain in the left thigh. Three months ago, a horse kicked him in the left midthigh, resulting in deep pain and swelling in the thigh muscles; x-ray was normal, and, over the next several days, the symptoms resolved with rest and ice packs. However, a few weeks later, the patient gradually developed recurrent pain and swelling in the same area. Vital signs are normal. Examination shows a solitary, hard, mobile, oval mass of approximately 4 × 5 cm in the anterior aspect of the left thigh. Excision of the mass is performed. Histologic examination is likely to show which of the following?

- ☒ A. Benign metaplastic bone with surrounding fibroblastic proliferation (49%)
- ☐ B. Closely packed, small, round, uniform neoplastic cells (2%)
- ☐ C. Mature adipocytes with focal large, atypical hyperchromatic cells (24%)
- ☐ D. Pleomorphic neoplastic spindle cells producing new woven bone (8%)
- ☐ E. Synovial cyst filled with gelatinous mucoid material (14%)



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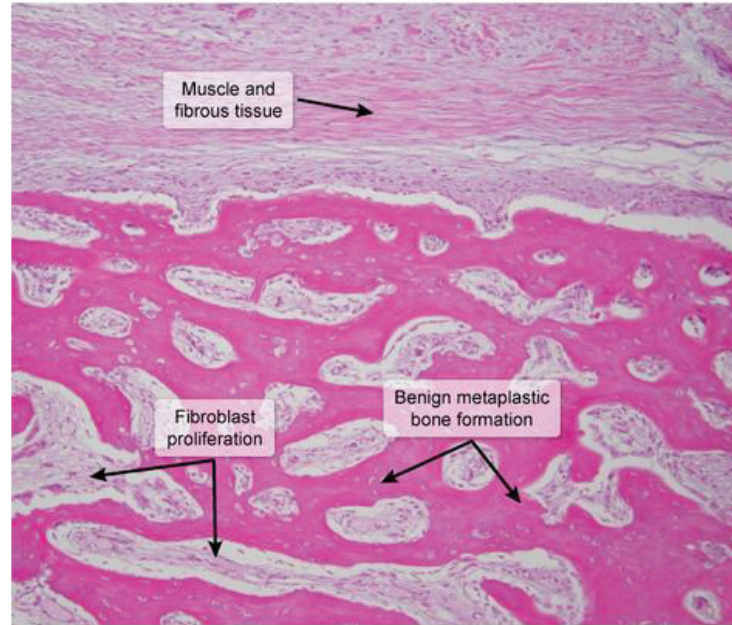
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End Block

Exhibit Display

Myositis ossificans



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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This patient likely has **myositis ossificans** (MO), characterized by the formation of lamellar bone in extraskeletal tissues (ie, **heterotopic ossification**). MO is typically triggered by severe (eg, fracture, muscle contusion) or recurrent **trauma** that initiates the expression of **bone morphogenic proteins**, which promote in-migration of spindle stem cells. These cells differentiate to fibroblasts (which produce collagen and extracellular matrix) and subsequently to chondrocytes and osteoblasts (which are responsible for production of osteoid and mineralization).

MO typically presents as a **painful, firm, mobile mass**. It is most common in the **quadriceps** and brachialis muscles but can occasionally occur in other muscles. X-ray typically shows **intramuscular calcification** with radiolucent zones (eggshell calcification). Histologic examination often shows a **zonal pattern** with outer areas of relatively mature bone (**benign metaplastic bone tissue**) and inner regions of **fibroblastic proliferation** (without mitotic atypia) and variable amounts of collagen and osteoid.

(Choice B) Closely packed, small, round, uniform neoplastic cells are a typical finding in **Ewing sarcoma**, which presents with bone pain and swelling, often accompanied by fever. Although it may occur in young adults, it is more common in children and is usually fixed to the bone, not mobile.

(Choice C) Mature adipocytes with large, atypical hyperchromatic cells are characteristic findings in



1



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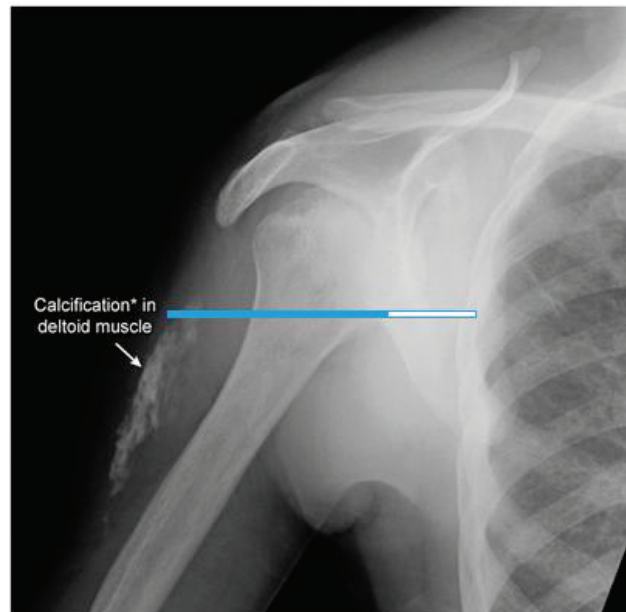
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Exhibit Display

Myositis ossificans



Calcification* in
deltoid muscle

*Heterotopic ossification at site of muscle injury

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Zoom In

Zoom Out

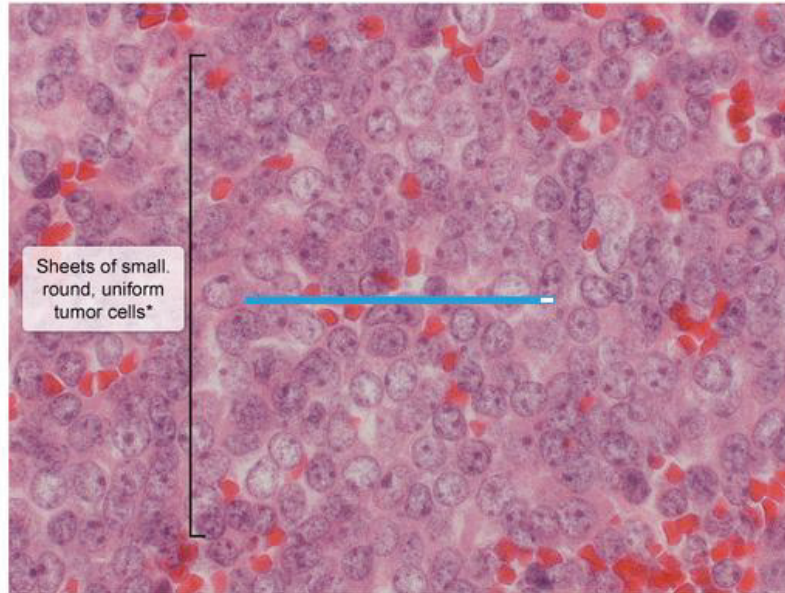
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Exhibit Display

Ewing sarcoma



Sheets of small, round, uniform tumor cells*

*Neuroectodermal cells with a high nuclear-cytoplasmic ratio.

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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adults, it is more common in children and is usually fixed to the bone, not mobile.

(Choice C) Mature adipocytes with large, atypical hyperchromatic cells are characteristic findings in [liposarcoma](#). These tumors can develop within the lower extremity muscles but are rare, typically occur at age >50, and are painless until they cause compression of surrounding structures.

(Choice D) Pleomorphic neoplastic spindle cells and new woven bone indicate [osteosarcoma](#). Although this occurs in patients age ≤ 20 years, the tumor usually arises in metaphysis (eg, distal femur, proximal tibia), and the mass is not mobile. In addition, this patient had no tumor 2 months ago on x-ray, and it is very unlikely for osteosarcoma to develop and progress within 2 months.

(Choice E) A ganglion cyst is an outpouching of synovial structures (eg, joint capsule, tendon sheath) filled with clear, gelatinous fluid. It presents as a painless, rubbery nodule, most commonly at the wrist or dorsal foot. The thigh muscle is not a common location.

Educational objective:

Myositis ossificans is characterized by the formation of lamellar bone in extraskeletal tissues (ie, heterotopic ossification), often triggered by trauma. It typically presents as a painful, firm, mobile mass within a muscle (eg, quadriceps). Histologic examination shows benign metaplastic bone and proliferating fibroblasts without mitotic atypia.



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Well differentiated liposarcoma

Mature adipocytes

Atypical adipocytes

D

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New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

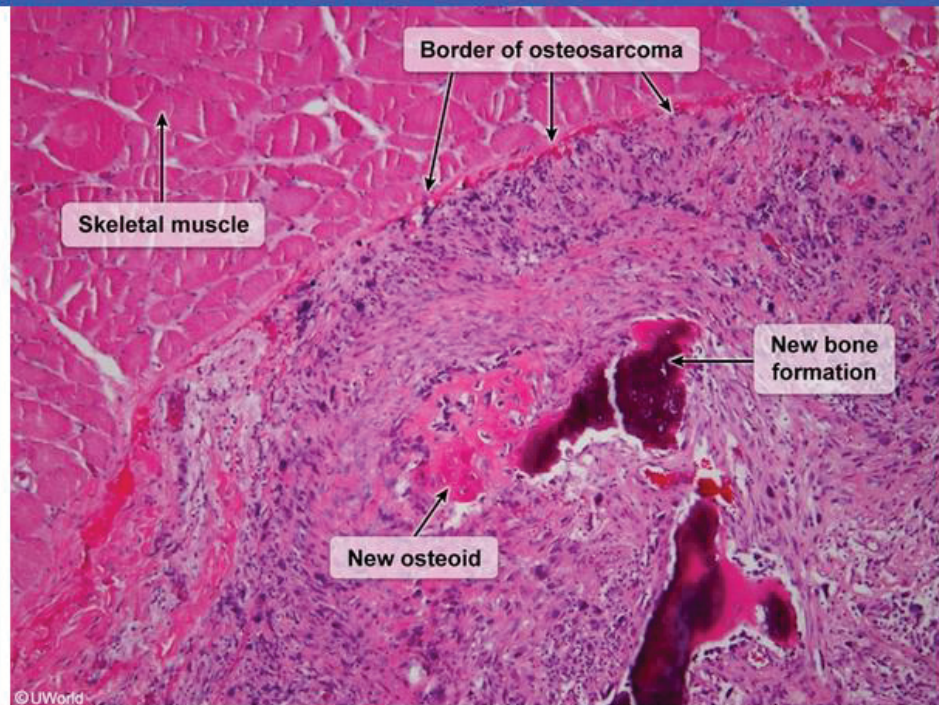
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Text Zoom

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fibroblasts without mitotic atypia

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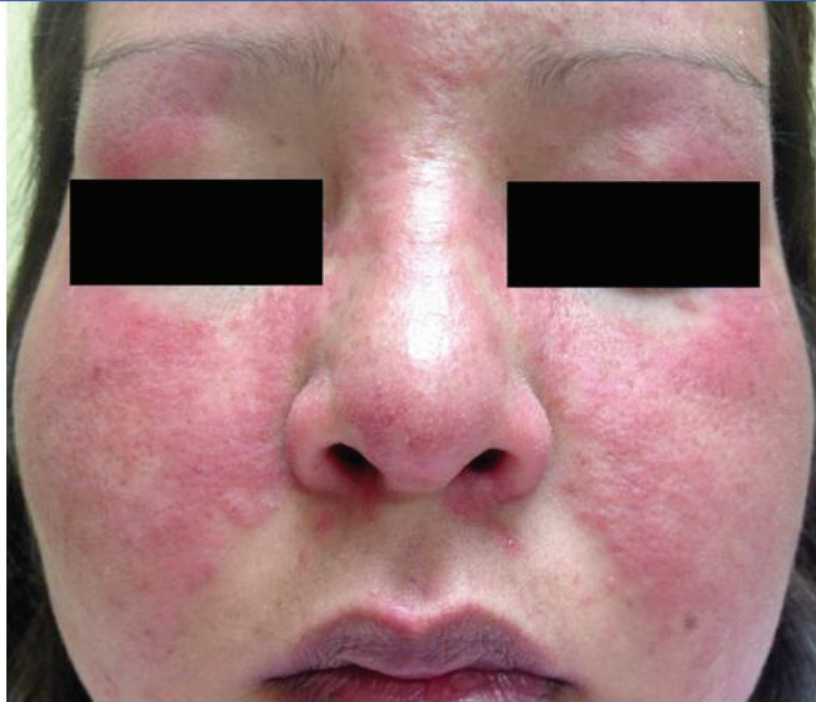
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A 30-year-old woman comes to the office due to a facial rash for the past 3 weeks. The rash worsens with sun exposure, and she has tried several topical sunscreens without relief. The patient also reports easy fatigability and occasional pain and swelling of her hand joints. Past medical history is notable for mild cervical dysplasia that was diagnosed at age 21 and resolved spontaneously. The patient does not use tobacco, alcohol or illicit drugs. Blood pressure is 140/85 mm Hg and pulse is 78/min. Physical examination reveals mucosal pallor, a superficial ulcer on the hard palate, and a rash as shown in the image below. Cardiopulmonary and abdominal examinations are normal.



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



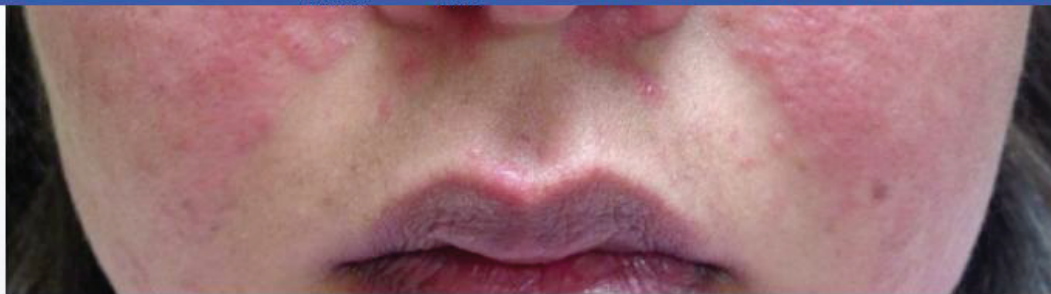
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Which of the following laboratory findings is most likely to be seen in this patient's condition?

- ☐ A. Decreased levels of complements C3 and C4
- ☐ B. Elevated titer of anti-cyclic citrullinated peptide antibodies
- ☐ C. Elevated titer of anti-mitochondrial antibodies
- ☐ D. Positive cervical swab culture for *Neisseria gonorrhoeae*
- ☐ E. Positive testing for human leukocyte antigen-B27

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



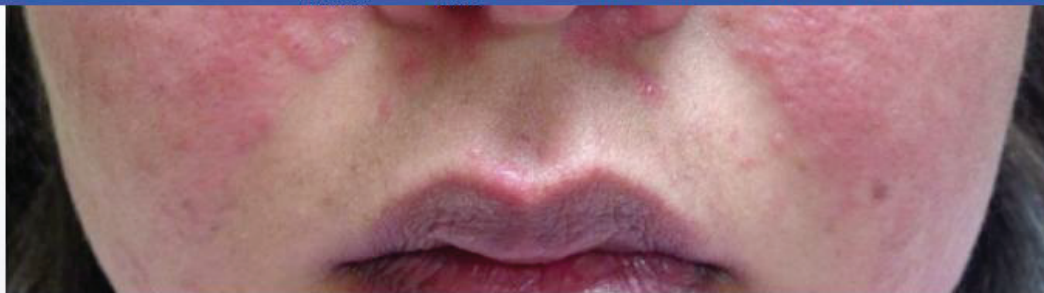
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Which of the following laboratory findings is most likely to be seen in this patient's condition?

- ☒ A. Decreased levels of complements C3 and C4 (58%)
- ☐ B. ~~Elevated titer of anti-cyclic citrullinated peptide antibodies (17%)~~
- ☐ C. ~~Elevated titer of anti-mitochondrial antibodies (13%)~~
- ☐ D. ~~Positive cervical swab culture for *Neisseria gonorrhoeae* (0%)~~
- ☐ E. Positive testing for human leukocyte antigen-B27 (9%)

Correct



58%

Answered correctly



01 min, 09 secs

Time Spent



11/24/2020

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Block Time Remaining: 00:36:45

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Systemic lupus erythematosus

| | |
|---------------------------------|---|
| Clinical presentation | <ul style="list-style-type: none">• Gradual symptom onset• Malar or discoid rash• Joint, renal, serosal &/or neurologic involvement |
| Laboratory abnormalities | <ul style="list-style-type: none">• Anemia, leukopenia, thrombocytopenia• Positive ANA, anti-double-stranded DNA, anti-Smith• Low complement levels, increased immune complexes |

ANA = antinuclear antibodies.

This patient has a photosensitive rash in the classic "butterfly" distribution at the malar region of the face, associated with inflammatory arthritis, and an **ulcer** at the hard palate. This constellation of clinical features is typical for new-onset **systemic lupus erythematosus** (SLE).

The central disturbance in SLE is excessive **autoantibody production** due to loss of self-tolerance. Autoantibodies directed against nuclear components (anti-nuclear antibodies) are the most characteristic feature of SLE. Autoantibody binding to self-antigens leads to the formation of circulating **immune complexes** that deposit in various organs and cause complement activation. Active SLE is therefore



Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

complexes that deposit in various organs and cause complement activation. Active SLE is therefore characterized by consumption of complement with **reduced** serum **complement levels**.

(Choice B) Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis (RA). RA causes an inflammatory arthritis, primarily affecting the small joints of the hands and wrists. Cutaneous manifestations of RA include subcutaneous nodules and leg ulcers, but a malar rash is more consistent with SLE.

(Choice C) Anti-mitochondrial antibodies are typically found in primary biliary cirrhosis, which typically presents with cholestatic symptoms (eg, pruritus, jaundice, malabsorption).

(Choice D) Disseminated gonococcal infection is characterized by fever, migratory polyarthritis, and skin lesions. The lesions are typically scattered pustules on the arms and legs and not a malar rash.

(Choice E) Human leukocyte antigen (HLA)-B27 is seen with increased frequency in the seronegative spondyloarthropathies (eg, ankylosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease, psoriatic arthritis).

Educational objectives:

Systemic lupus erythematosus is characterized by loss of immune self-tolerance with production of





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

causes an inflammatory arthritis, primarily affecting the small joints of the hands and wrists. Cutaneous manifestations of RA include subcutaneous nodules and leg ulcers, but a malar rash is more consistent with SLE.

(Choice C) Anti-mitochondrial antibodies are typically found in primary biliary cirrhosis, which typically presents with cholestatic symptoms (eg, pruritus, jaundice, malabsorption).

(Choice D) Disseminated gonococcal infection is characterized by fever, migratory polyarthritis, and skin lesions. The lesions are typically scattered pustules on the arms and legs and not a malar rash.

(Choice E) Human leukocyte antigen (HLA)-B27 is seen with increased frequency in the seronegative spondyloarthropathies (eg, ankylosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease, psoriatic arthritis).

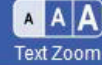
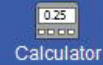
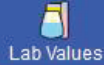
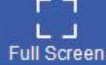
Educational objectives:

Systemic lupus erythematosus is characterized by loss of immune self-tolerance with production of autoantibodies against nuclear antigens. Binding of autoantibodies to self antigens leads to deposition of immune complexes in tissues and consumption of complement.

References

- [The pathogenesis of systemic lupus erythematosus-an update.](#)





A 59-year-old man comes to the office due to progressive weakness for the past several weeks. The patient has had difficulty getting out of bed and climbing stairs in the morning, which improves gradually as he "warms up the muscles" with continued use. He has also had to drink water more frequently due to dry mouth and has had episodic double vision. The patient also reports difficulty achieving erections despite having a good libido. Neurologic examination shows decreased strength of the hip flexors and diminished knee reflexes. Repeat examination after lower extremity isometric exercise shows normalization of the muscle strength and deep tendon reflexes. Which of the following conditions is most closely associated with this patient's current disease process?

- ☐ A. *Campylobacter jejuni* enteritis
- ☐ B. Gastric adenocarcinoma
- ☐ C. Giant cell arteritis
- ☐ D. Medullary thyroid cancer
- ☐ E. Small cell lung cancer
- ☐ F. Thymic neoplasia





he "warms up the muscles" with continued use. He has also had to drink water more frequently due to dry mouth and has had episodic double vision. The patient also reports difficulty achieving erections despite having a good libido. Neurologic examination shows decreased strength of the hip flexors and diminished knee reflexes. Repeat examination after lower extremity isometric exercise shows normalization of the muscle strength and deep tendon reflexes. Which of the following conditions is most closely associated with this patient's current disease process?

- ☐ A. *Campylobacter jejuni* enteritis (7%)
- ☐ B. Gastric adenocarcinoma (1%)
- ☐ C. Giant cell arteritis (6%)
- ☐ D. Medullary thyroid cancer (3%)
- ☒ E. Small cell lung cancer (70%)
- ☐ F. Thymic neoplasia (9%)

Correct

70%



49 secs



02/21/2021

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1



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Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Autoimmune-mediated neuromuscular junction disorders

| | Myasthenia gravis | Lambert-Eaton myasthenic syndrome |
|------------------------------|---|---|
| Antibodies | Acetylcholine receptor antibody | Voltage-gated calcium channel antibody |
| Location of defect | Postsynaptic | Presynaptic |
| Weakness | Extraocular & bulbar affected first (eg, ptosis, diplopia) | Proximal muscles affected first (eg, weakness standing from chair) |
| Deep-tendon reflexes | Intact | Decreased/absent |
| Autonomic dysfunction | Rare | Common |
| Association | Thymoma/thymic hyperplasia | Malignancy (eg, small cell lung cancer) |



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Feedback



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| Association | Thymoma/thymic hyperplasia | Malignancy (eg, small cell lung cancer) |
|-----------------------------|----------------------------|---|
| Tensilon test (edrophonium) | Improves weakness | No change |
| Response to exercise | Decreased strength | Increased strength |
| Nerve stimulation studies | Decremental response | Incremental response |

This patient with proximal muscle weakness and decreased deep tendon reflexes that improve with exercise has **Lambert-Eaton myasthenic syndrome (LEMS)**. LEMS is an immune-mediated disorder of the neuromuscular junction characterized by **autoantibodies** directed at the **presynaptic voltage-gated calcium channel**, resulting in decreased acetylcholine release and muscle weakness. LEMS is strongly associated with **small cell lung cancer**, likely due to the immune recognition of voltage-gated calcium channels that are present on the malignant cells.

Patients typically develop progressive **proximal muscle weakness** that manifests in the form of gait alteration and difficulty arising from a chair or climbing stairs. **Autonomic symptoms**, such as dry mouth or impotence, are common. Cranial nerve (particularly ptosis) and respiratory muscle involvement may



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

or impotence, are common. Cranial nerve (particularly ptosis) and respiratory muscle involvement may occur but typically manifest later in the disease course. Patients may experience **postexercise facilitation**, in which muscle strength and deep tendon reflexes improve with exercise or repetitive movements (due to accumulation of calcium within the axon terminal). This effect is also seen in repetitive nerve stimulation studies.

(Choice A) Guillain-Barré syndrome is an acute postinfectious polyneuropathy often associated with *Campylobacter jejuni* infections. It is characterized by rapidly progressive, ascending paralysis that does not improve with repetitive movement.

(Choice B) Paraneoplastic syndromes associated with gastric adenocarcinoma include abrupt onset of numerous seborrheic keratoses (**Leser-Trélat sign**) and **acanthosis nigricans**.

(Choice C) Giant cell arteritis is characterized by headache, visual changes, and jaw claudication in older adults. It is not associated with LEMS.

(Choice D) Medullary thyroid cancer may be associated with multiple endocrine neoplasia (MEN) type 2 (both A and B variants). MEN 2A is associated with pheochromocytoma and hyperparathyroidism, whereas MEN 2B is associated with pheochromocytoma and mucosal neuromas.

(Choice E) Thymic neoplasia or thymomas are commonly associated with myasthenia gravis (MG).



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Feedback



Suspend



End Block

Exhibit Display



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Zoom Out

Reset

New | Existing

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(Choice E) Thymic neoplasia or thymomas are commonly associated with myasthenia gravis (MG)

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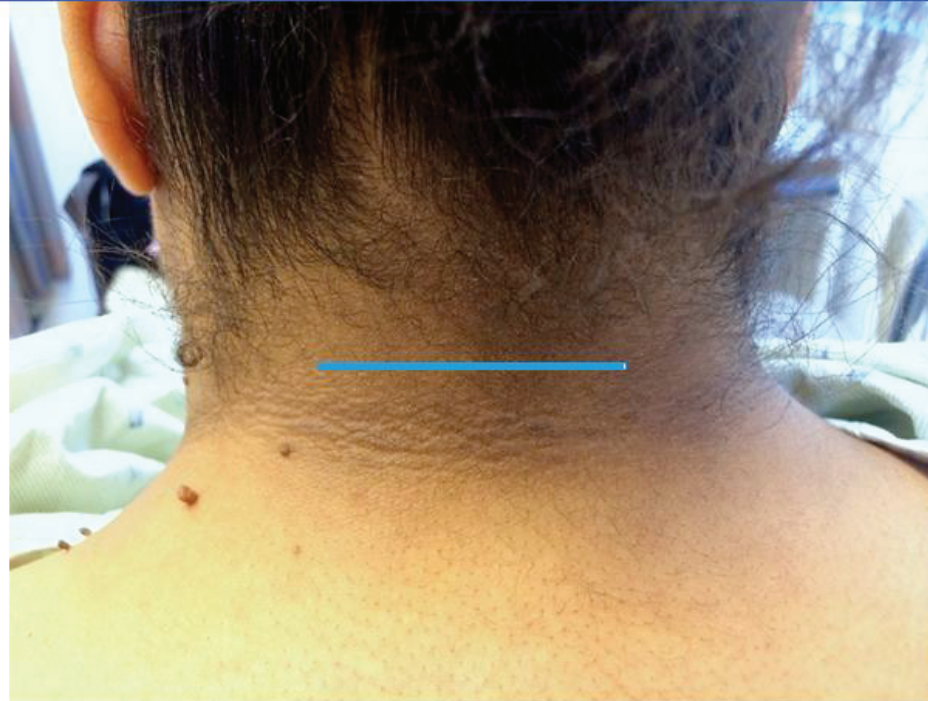


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Suspend

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(Choice E) Thymic neoplasia or thymomas are commonly associated with myasthenia gravis (MG)

Block Time Remaining: 00:37:34

TUTOR

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Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

adults. It is not associated with LEMS.

(Choice D) Medullary thyroid cancer may be associated with multiple endocrine neoplasia (MEN) type 2 (both A and B variants). MEN 2A is associated with pheochromocytoma and hyperparathyroidism, whereas MEN 2B is associated with pheochromocytoma and mucosal neuromas.

(Choice F) Thymic neoplasia or thymomas are commonly associated with myasthenia gravis (MG), another autoimmune neuromuscular condition. MG is often confused with LEMS; however, in MG facial, periocular, and bulbar weakness typically presents before extremity weakness. In addition, the weakness worsens with exercise, deep tendon reflexes typically remain intact, and autonomic dysfunction is rare.

Educational objective:

Lambert-Eaton myasthenic syndrome (LEMS) is a neuromuscular disorder characterized by autoantibodies against presynaptic voltage-gated calcium channels. It causes progressive proximal muscle weakness and decreased deep tendon reflexes that improve with exercise (postexercise facilitation); cranial nerve involvement and autonomic symptoms may also occur. LEMS is strongly associated with small cell lung cancer.

Pathology

Rheumatology/Orthopedics & Sports

Eaton lambert myasthenic syndrome

Subject

System

Topic

Block Time Remaining: 00:37:34

TUTOR

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 24-year-old woman comes to the office due to a persistent facial rash. The patient easily develops "sunburns" after sun exposure and her fingers "turn blue" in cold weather. She has also felt more fatigued than usual. Physical examination shows a facial rash in a butterfly distribution that spares the nasolabial folds. Laboratory studies reveal several types of autoantibodies directed against components of the cell nucleus. One specific antibody targets proteins complexed with small nuclear ribonucleic acid. These protein-ribonucleic acid complexes are most likely involved in which of the following cellular functions?

- ☐ A. Aiding mRNA in exiting the nucleus
- ☐ B. Allowing proper functioning of DNA ligase
- ☐ C. Charging tRNA with amino acids
- ☐ D. Polyadenylation of RNA transcripts
- ☐ E. Removal of introns from RNA transcripts
- ☐ F. Synthesizing Okazaki fragments

Submit

Block Time Remaining: 00:37:35

TUTOR

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Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 24-year-old woman comes to the office due to a persistent **facial rash**. The patient easily develops "sunburns" after sun exposure and her fingers **"turn blue"** in cold weather. She has also felt more fatigued than usual. Physical examination shows a facial rash in a **butterfly** distribution that spares the nasolabial folds. Laboratory studies reveal several types of autoantibodies directed against components of the cell nucleus. One specific antibody targets proteins complexed with small nuclear ribonucleic acid. These protein-ribonucleic acid complexes are most likely involved in which of the following cellular functions?

- ☐ A. Aiding mRNA in exiting the nucleus (12%)
- ☐ B. ~~Allowing proper functioning of DNA ligase (5%)~~
- ☐ C. ~~Charging tRNA with amino acids (8%)~~
- ☐ D. ~~Polyadenylation of RNA transcripts (5%)~~
- ☒ E. Removal of introns from RNA transcripts (64%)
- ☐ F. Synthesizing Okazaki fragments (3%)



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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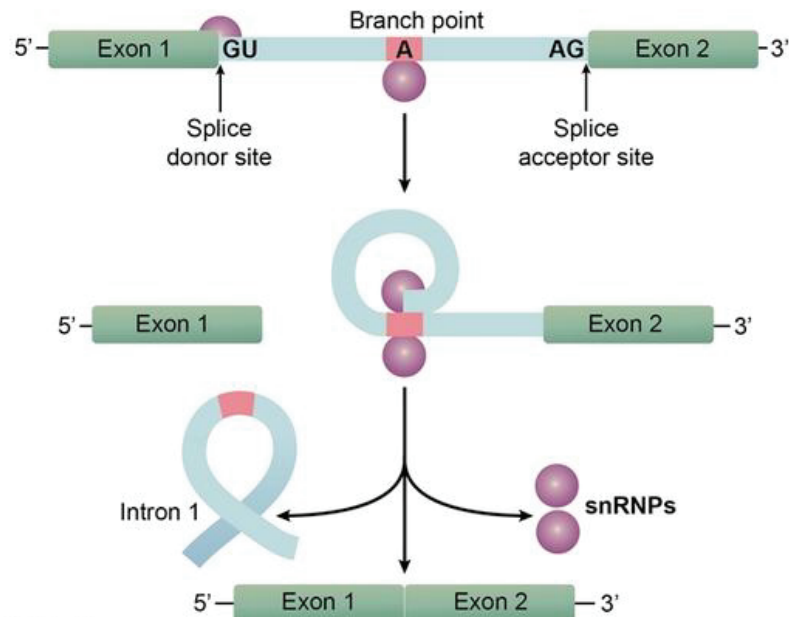
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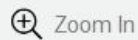
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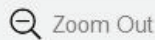
Splicing of pre-mRNA



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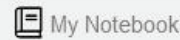
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Feedback



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's constellation of symptoms (eg, malar rash, photosensitivity, Raynaud phenomenon ["blue fingers"], fatigue) is consistent with systemic lupus erythematosus, an autoimmune disease associated with anti-Smith antibodies (highly specific). Smith protein normally complexes with small nuclear RNA (snRNA) in the cytoplasm, forming small nuclear ribonucleoproteins (snRNPs).

Transcription occurs in the nucleus and is catalyzed by 3 types of **RNA polymerases**, leading to the formation of messenger RNA (mRNA), ribosomal RNA (rRNA), transport RNA (tRNA), and snRNA. **RNA polymerase II** synthesizes both mRNA and **snRNA**, the latter of which combines with specific proteins to form **snRNPs**. mRNA synthesis occurs in 2 stages. During the first, the DNA template is transcribed into a complementary strand of pre-mRNA. In the second, pre-mRNA is processed into mature mRNA through the following steps:

1. RNA capping: Addition of a methylated guanine nucleotide to the 5' end.
2. RNA polyadenylation: Addition of several adenine nucleotides to the 3' end (poly-A tail).
3. RNA splicing: **Removal of introns** (noncoding regions) by **spliceosomes**, which consist of snRNPs and other proteins.

Mature mRNA then transfers the genetic code to the cytoplasm and serves as a template for protein synthesis (translation).



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom

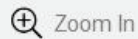


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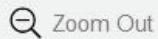
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| Synthesis & function of eukaryotic RNA | | |
|--|-------------------------------|---|
| Synthesizing polymerase | Type of RNA produced | Function |
| RNA polymerase I | 18S, 5.8S & 28S ribosomal RNA | Form essential ribosomal components |
| RNA polymerase II | Messenger RNA | Translated by ribosomes to form specific proteins |
| | Small nuclear RNA | Involved in mRNA splicing & transcription regulation |
| | Micro RNA | Cause gene silencing via translation arrest or mRNA degradation |
| RNA polymerase III | Transfer RNA | Adaptor molecule linking codons with specific amino acids |
| | 5S ribosomal RNA | Essential component of 60S ribosomal subunit |

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New

| Existing



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synthesis (translation).

(Choices A and D) Polyadenylation of RNA transcripts is performed by the enzyme polyadenylate polymerase. This process stabilizes mRNA, helping it exit the nucleus.

(Choices B and F) During eukaryotic DNA replication, DNA polymerase δ elongates Okazaki fragments of the lagging strand. These Okazaki fragments are later joined by the enzyme DNA ligase.

(Choice C) During translation, aminoacyl-tRNA synthetases catalyze the linkage of tRNAs to their corresponding amino acids. Each enzyme recognizes a specific amino acid and all of the tRNAs that match that amino acid.

Educational objective:

Small nuclear RNA (snRNA) is synthesized by RNA polymerase II in the nucleus and complexes with specific proteins to form small nuclear ribonucleoproteins (snRNPs). snRNPs are an essential component of spliceosomes, which remove introns from pre-mRNA to form mature mRNA. Patients with systemic lupus erythematosus can have autoantibodies directed against snRNPs (eg, anti-Smith antibody).

References

- [Spliceosome structure and function.](#)
- [Anti-Sm and anti-RNP antibodies.](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 50-year-old man comes to the office for evaluation of a nodule in his palm just proximal to the third metacarpophalangeal joint. It has grown larger since it first appeared several months ago and he now has mild flexion of the finger, which he is unable to straighten. The patient reports that his mother had similar problems with her fingers. Examination of the affected hand is shown in the [exhibit](#). Which of the following pathologic processes is most likely involved in this patient's condition?

- ☐ A. Fibroblastic proliferation and thickening of palmar fascia
- ☐ B. Heterotopic bone formation within lumbrical muscles
- ☐ C. Linear deposits of calcium hydroxyapatite
- ☐ D. Mucinous, gelatinous fluid filling of the tendon sheath
- ☐ E. Neutrophilic infiltration of flexor tendons

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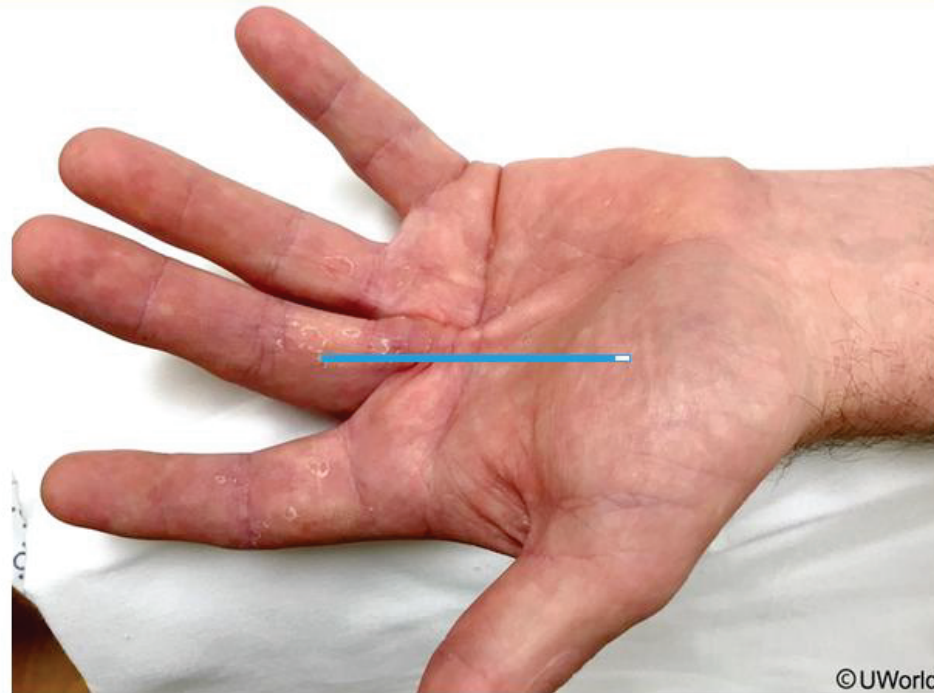


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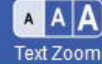
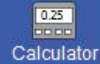
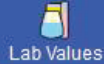
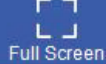


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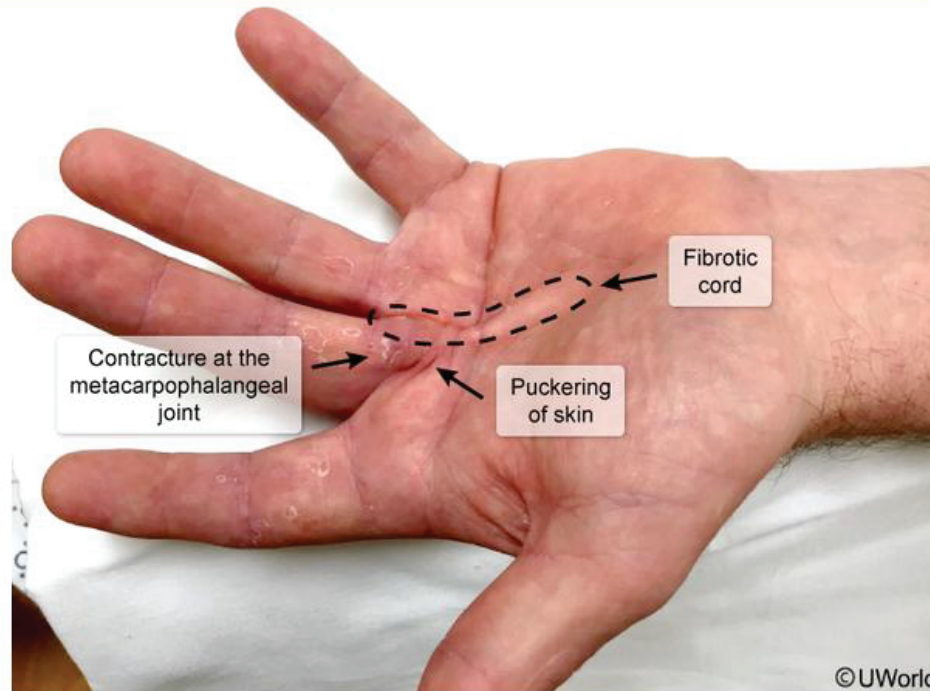


A 50-year-old man comes to the office for evaluation of a **nodule** in his palm just proximal to the third metacarpophalangeal joint. It has grown larger since it first appeared several months ago and he now has mild flexion of the finger, which he is unable to straighten. The patient reports that his mother had similar problems with her fingers. Examination of the affected hand is shown in the **exhibit**. Which of the following pathologic processes is most likely involved in this patient's condition?

- ☒ A. Fibroblastic proliferation and thickening of palmar fascia (69%)
- ☐ B. ~~Heterotopic bone formation within lumbrical muscles (5%)~~
- ☐ C. ~~Linear deposits of calcium hydroxyapatite (5%)~~
- ☐ D. ~~Mucinous, gelatinous fluid filling of the tendon sheath (12%)~~
- ☒ E. Neutrophilic infiltration of flexor tendons (6%)

IncorrectCorrect answer
A 69%
Answered correctly 01 min, 13 secs
Time Spent 01/20/2021
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Mark



Previous



Next



Full Screen



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Notes



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This patient has **Dupuytren contracture** (DC), a condition caused by **progressive fibrosis** of the superficial **palmar fascia**. The disease typically involves the fascia at the base of the middle, ring, and little fingers. Although the etiology of DC is unknown, risk factors include age >50, male sex, **family history**, and Northern European ancestry.

DC is thought to be caused by overstimulation of the Wnt-signaling pathway, which regulates cellular proliferation. Initial findings include painless **fascial thickening** with puckering of the skin just proximal to the affected metacarpophalangeal joint(s). As fibrosis continues, pathognomonic fascial **nodules** form along the flexor tendons composed of **proliferating fibroblasts** and disordered type III collagen. The nodules eventually coalesce into palpable **fibrotic cords** that tether the flexor tendon to the palmar fascia, leading to **loss of finger extension** (ie, contractures) at the metacarpophalangeal and proximal interphalangeal joints.

(Choice B) Heterotopic bone formation in muscles is characteristic of **myositis ossificans**, a benign condition that develops after contusion to large muscle groups (eg, quadriceps femoris), not small muscles such as the lumbricals. Patients typically report pain in the affected muscle and a palpable lump (ie, heterotopic bone) deep in the muscle.



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

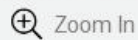
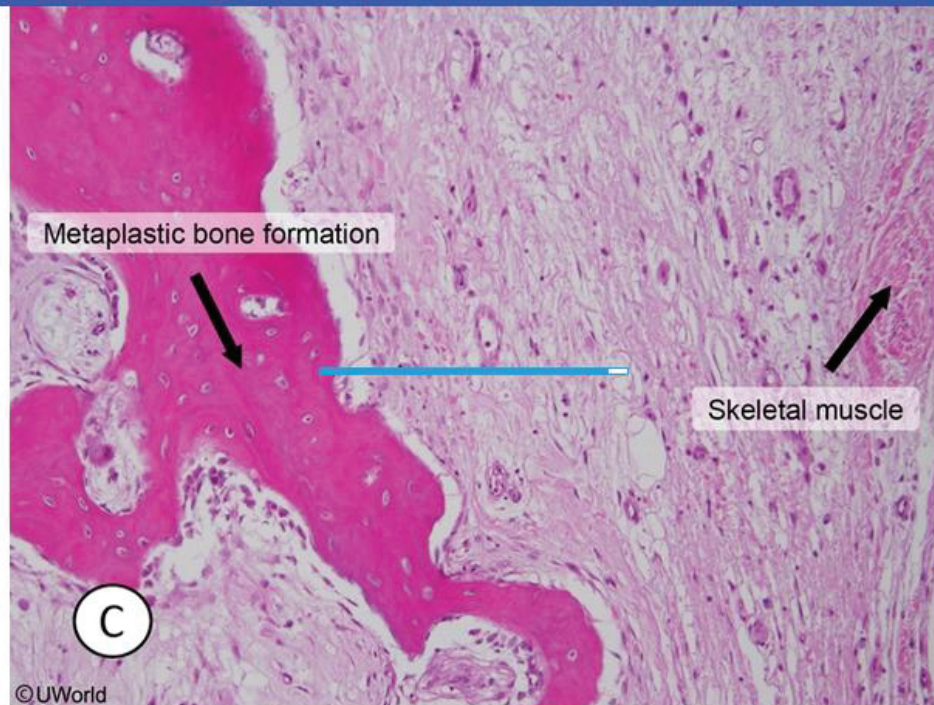


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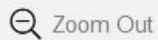


Settings

Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



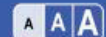
Notes



Calculator



Reverse Color



Text Zoom



Settings

heterotopic bone) deep in the muscle.

(Choice C) Linear deposits of calcium hydroxyapatite in the periarticular structures cause a painful inflammatory condition called calcific peritendinitis. However, it usually affects the rotator cuff; hand and wrist involvement is uncommon and would present with associated inflammatory changes (eg, redness, swelling, warmth).

(Choice D) Mucinous, gelatinous fluid filling of the tendon sheath is characteristic of a [ganglion cyst](#). Unlike fibrotic nodules in DC, ganglion cysts present as large, mobile, rubbery nodules that do not lead to contractures of the hand.

(Choice E) Neutrophilic infiltration of tendon sheaths is characteristic of bacterial tenosynovitis. Because it is an inflammatory condition, it presents with significant redness, warmth, and swelling, none of which are present in DC.

Educational objective:

Dupuytren contracture is caused by progressive fibrosis of the superficial palmar fascia due to excessive fibroblast proliferation. Pathognomonic fibrotic nodules and cords form along the flexor tendons, limiting extension of the affected digits.

References



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



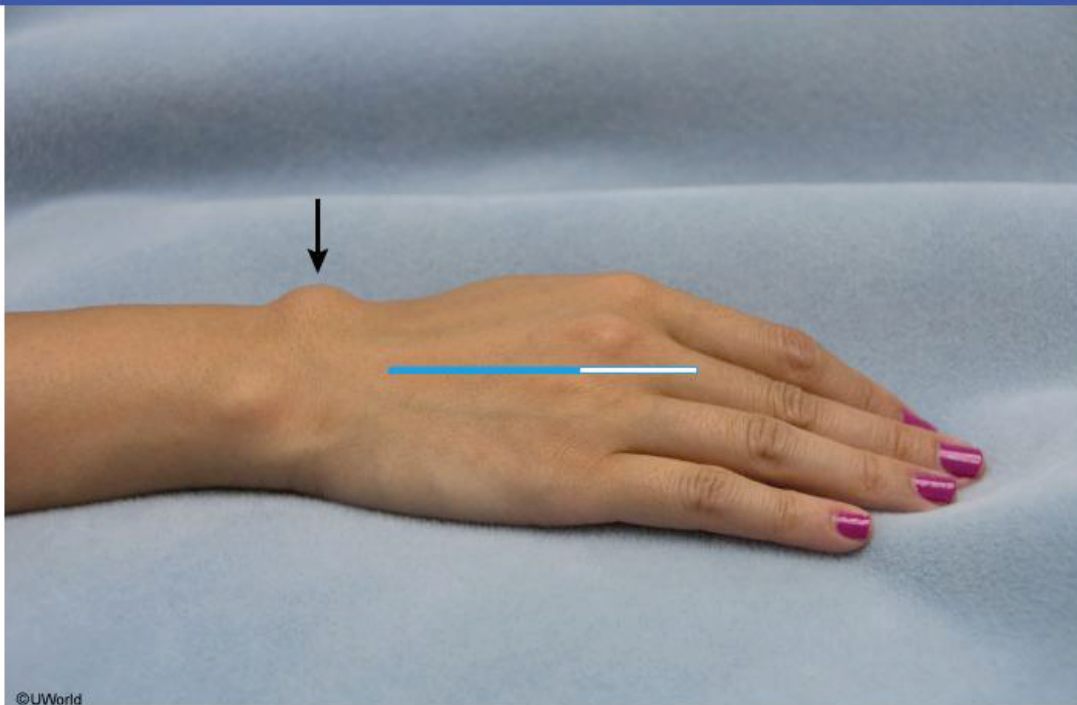
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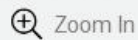
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metastatic bone) deep in the muscle.

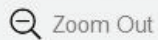
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Zoom In



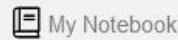
Zoom Out



Reset



New | Existing



My Notebook



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 28-year-old man comes to the emergency department due to 12 hours of severe right knee pain and swelling. He has had no trauma. The patient drinks 1 or 2 cans of beer on weekends but does not use tobacco or illicit drugs. On physical examination, right knee effusion, erythema, and tenderness are present. Active and passive range of motion is markedly decreased. Other joints are normal.

Arthrocentesis is performed, and synovial fluid analysis shows a white blood cell count of 110,000/mm³.

Which of the following would provide the best treatment for this patient's condition?

- ☐ A. Allopurinol
- ☐ B. Antibiotics
- ☐ C. Colchicine
- ☐ D. Indomethacin
- ☐ E. Prednisone

Submit

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Feedback



Suspend



End Block



A 28-year-old man comes to the emergency department due to 12 hours of severe right knee pain and swelling. He has had no trauma. The patient drinks 1 or 2 cans of beer on weekends but does not use tobacco or illicit drugs. On physical examination, right knee effusion, erythema, and tenderness are present. Active and passive range of motion is markedly decreased. Other joints are normal. Arthrocentesis is performed, and synovial fluid analysis shows a white blood cell count of 110,000/mm³. Which of the following would provide the best treatment for this patient's condition?

- ☐ A. Allopurinol (2%)
- ☒ B. Antibiotics (71%)
- ☐ C. Colchicine (7%)
- ☐ D. Indomethacin (11%)
- ☐ E. Prednisone (7%)

Correct

 71%
Answered correctly 43 secs
Time Spent 12/18/2020
Last Updated

Block Time Remaining: 00:40:55

TUTOR

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Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient has acute monoarticular arthritis with an effusion, decreased range of motion of the affected joint, and a synovial fluid leukocyte count $>100,000/\text{mm}^3$. **Septic arthritis** (very often due to gonococcus in this patient's age group) is a likely diagnosis, and he should receive antibiotics given the risk of joint destruction, osteomyelitis, and sepsis. Synovial fluid Gram stain and culture can help confirm the diagnosis (although cultures can sometimes be negative with gonococcus). Microscopy can exclude the presence of crystals suggestive of gout and pseudogout, conditions that can also cause acute monoarticular arthritis (gout is associated with alcohol use). However, they typically present at an older age, and the synovial fluid leukocyte count is usually lower (at the lower end of the $20,000\text{-}100,000/\text{mm}^3$ range).

(Choice A) Allopurinol is a hypoxanthine isomer that lowers serum uric acid levels. It is prescribed to prevent attacks of acute gouty arthritis but is not useful in the treatment of acute flares.

(Choices C, D, and E) Colchicine reduces the acute inflammation of gouty arthritis by inhibiting neutrophil migration into the inflamed areas. Indomethacin, a nonsteroidal anti-inflammatory drug (NSAID), may be prescribed for pain relief in noninfectious inflammatory arthritis (eg, gout) but would not treat infection. Prednisone is sometimes used in the treatment of gout when there are contraindications to colchicine and NSAIDs.

Educational objective:



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(gout is associated with alcohol use). However, they typically present at an older age, and the synovial fluid leukocyte count is usually lower (at the lower end of the 20,000-100,000/mm³ range).

(Choice A) Allopurinol is a hypoxanthine isomer that lowers serum uric acid levels. It is prescribed to prevent attacks of acute gouty arthritis but is not useful in the treatment of acute flares.

(Choices C, D, and E) Colchicine reduces the acute inflammation of gouty arthritis by inhibiting neutrophil migration into the inflamed areas. Indomethacin, a nonsteroidal anti-inflammatory drug (NSAID), may be prescribed for pain relief in noninfectious inflammatory arthritis (eg, gout) but would not treat infection. Prednisone is sometimes used in the treatment of gout when there are contraindications to colchicine and NSAIDs.

Educational objective:

A high synovial fluid leukocyte count (>100,000/mm³) and absent crystals on microscopic examination strongly suggest bacterial joint infection. Septic arthritis requires antibiotic treatment to prevent joint destruction, osteomyelitis, and sepsis.

Pathology

Rheumatology/Orthopedics & Sports

Septic arthritis

Subject

System

Topic



0



Feedback



Suspend



End Block

A 68-year-old man comes to the office due to difficulty performing normal day-to-day activities with his hands. He has had pain in his finger joints, wrists, and knees for many years and has been taking over-the-counter analgesics. The patient has been evaluated by doctors for "joint problems" in the past but declined their treatment recommendations. He has smoked a pack of cigarettes daily for 30 years. Vital signs are normal. Examination findings of the patient's hands are shown in the image below.





Which of the following pathogenic mechanisms is most likely responsible for this patient's condition?

- ☐ A. Calcific degeneration of the cartilage
- ☐ B. Cartilage thinning and subchondral sclerosis
- ☐ C. DNA/anti-DNA immune complex deposition
- ☐ D. Synovial pannus formation
- ☐ E. Uric acid crystal deposition

Submit

Block Time Remaining: 00:41:01

TUTOR

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Feedback

Suspend

End Block



Which of the following pathogenic mechanisms is most likely responsible for this patient's condition?

- ☐ A. Calcific degeneration of the cartilage (4%)
- ☐ B. Cartilage thinning and subchondral sclerosis (12%)
- ☐ C. DNA/anti-DNA immune complex deposition (8%)
- ☒ D. Synovial pannus formation (73%)
- ☐ E. Uric acid crystal deposition (0%)

Correct

73%

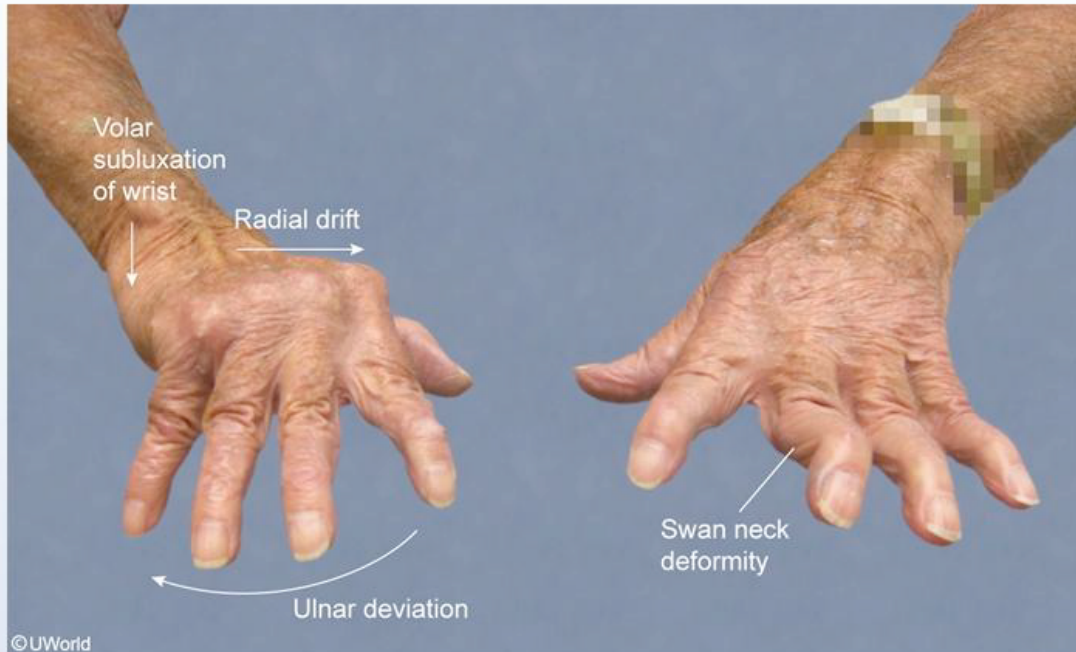
44 secs

03/05/2021

Block Time Remaining: 00:41:39
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This patient has a chronic, symmetric, deforming arthritis consistent with **advanced rheumatoid arthritis** (RA). His examination shows classic features including joint enlargement, **ulnar deviation** at the metacarpophalangeal joints, and **swan neck deformities** (hyperextension at the proximal interphalangeal



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Ulnar deviation

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This patient has a chronic, symmetric, deforming arthritis consistent with **advanced rheumatoid arthritis** (RA). His examination shows classic features including joint enlargement, **ulnar deviation** at the metacarpophalangeal joints, and **swan neck deformities** (hyperextension at the proximal interphalangeal joints with flexion at the distal interphalangeal joints).

The joint destruction in RA is thought to be initiated by CD4+ T helper cells and is characterized by **synovial hyperplasia** and an **inflammatory infiltrates** (often containing lymphoid follicles). The joint space often becomes replaced by a **synovial pannus**, an invasive mass composed of fibroblast-like synovial cells, granulation tissue, and inflammatory cells. Release of proteinases (eg, matrix metalloproteinase 13) causes **destruction** of the articular cartilaginous matrix, facilitating erosion of the surrounding **articular cartilage** and underlying bone. Ossification of the pannus can lead to fusion of the bones across the affected joint (bony ankylosis).

(Choices A and E) Calcific degeneration of the articular cartilage (chondrocalcinosis) is a characteristic feature of calcium pyrophosphate dihydrate deposition disease (pseudogout). Deposition of uric acid crystals results in gout. Both gout and pseudogout are inflammatory arthritides that can cause pain and joint deformation but present with acute, episodic arthritis and are more common in the lower extremities.



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Feedback



Suspend



End Block



joint deformation but present with acute, episodic arthritis and are more common in the lower extremities.

(Choice B) Osteoarthritis is characterized by progressive fracturing and erosion of the articular cartilage.

Periarticular findings include osteophyte formation and subchondral sclerosis. When osteoarthritis affects the hands, it typically presents with bony enlargement at the proximal and distal interphalangeal joints (Bouchard and Heberden nodes, respectively) rather than ulnar deviation at the metacarpophalangeal joints.

(Choice C) Autoimmune complex deposition (type III hypersensitivity) plays a significant role in the arthritis associated with systemic lupus erythematosus. Although lupus may cause a chronic destructive arthritis resembling RA in a minority of cases, lupus arthritis is typically migratory, nondeforming, and much more common in younger women than in older men.

Educational objective:

Joint destruction in rheumatoid arthritis is characterized by synovial hyperplasia, an inflammatory infiltrate, and synovial angiogenesis. The joint space often becomes replaced by pannus, an invasive mass composed of fibroblast-like synovial cells, granulation tissue, and inflammatory cells that can erode into the articular cartilage and underlying bone.

Pathology

Rheumatology/Orthopedics & Sports

Rheumatoid arthritis

Block Time Remaining: 00:41:39

TUTOR

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



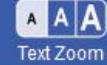
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 32-year-old woman complains of weakness in her hands and "heaviness" in her eyelids at the end of each day. Chest imaging shows an anterior mediastinal mass. The organ from which this mass most likely originated shares its embryologic origin with:

- ☐ A. Thyroid gland
- ☐ B. Superior parathyroid glands
- ☐ C. Inferior parathyroid glands
- ☐ D. Larynx
- ☐ E. Palatine tonsils

Submit

1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 32-year-old woman complains of weakness in her hands and "heaviness" in her eyelids at the end of each day. Chest imaging shows an **anterior mediastinal mass**. The organ from which this mass most likely originated shares its embryologic origin with:

- ☐ A. Thyroid gland (22%)
- ☐ B. Superior parathyroid glands (16%)
- ☒ C. Inferior parathyroid glands (46%)
- ☐ D. Larynx (5%)
- ☐ E. Palatine tonsils (8%)

Correct

46%

Answered correctly



36 secs

Time Spent



01/30/2021

Last Updated

Explanation



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



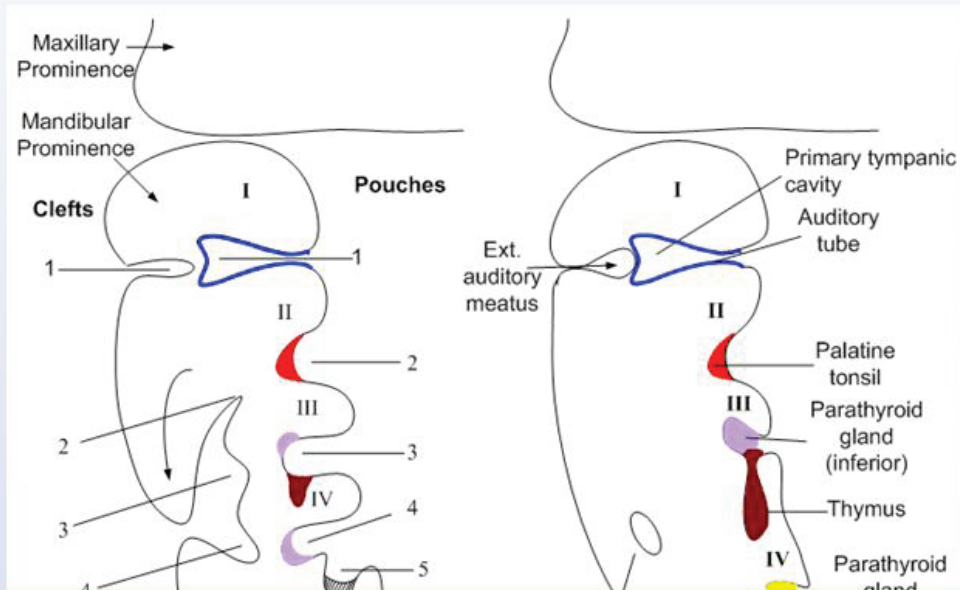
Text Zoom



Settings

Myasthenia gravis causes muscle weakness, with the extraocular muscles most commonly affected.

Patients often experience ptosis and diplopia. The muscle weakness worsens with activity, and patients often note that their symptoms are worse at the end of the day. The majority of patients with myasthenia gravis are found to have a thymoma or thymic hyperplasia.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

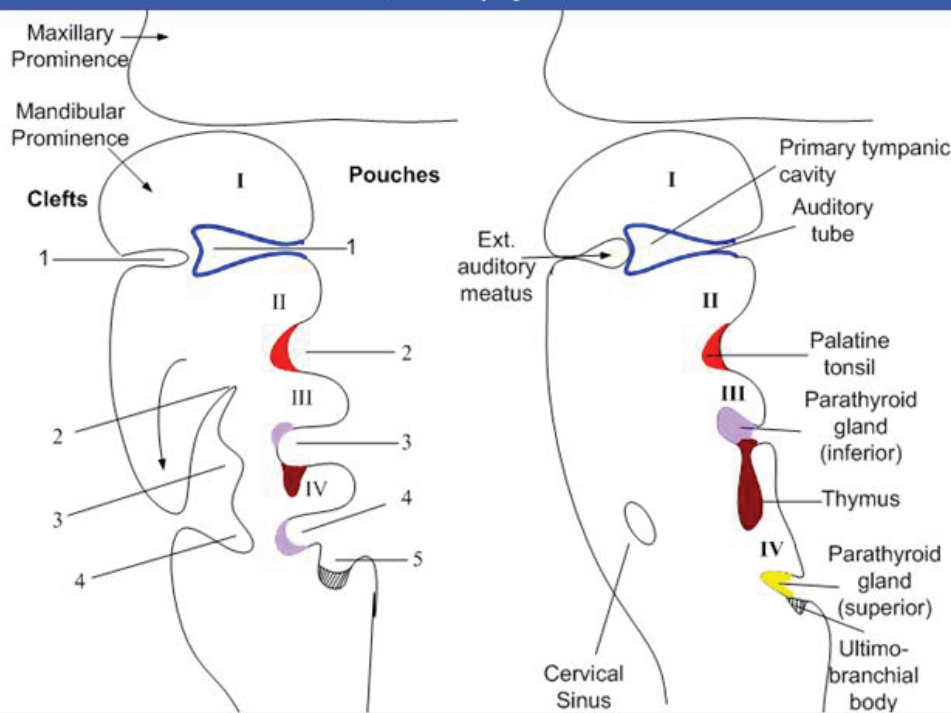
Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The thymus is derived from the third pharyngeal pouch, as are the inferior parathyroid glands. The table below lists the derivatives of the pharyngeal pouches, grooves and membranes:

| | Pharyngeal pouch | Pharyngeal membrane | Pharyngeal groove |
|---|--|---------------------|----------------------------------|
| 1 | Epithelium of middle ear and auditory tube | Tympanic membrane | Epithelium of external ear canal |
| 2 | Epithelium of palatine tonsil crypts | Obliterated | |
| 3 | Thymus, inferior parathyroid glands | Obliterated | |
| 4 | Superior parathyroid glands, | Obliterated | |



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

4

Superior
parathyroid
glands,
ultimobranchial
body

Obliterated

(Choice A) The floor of the foregut gives rise to the thyroid diverticulum. The thyroid diverticulum migrates caudally to the neck, but remains attached to the floor of the mouth by the thyroglossal duct.

(Choice B) The superior parathyroid glands and ultimobranchial body are formed from the 4th pharyngeal pouch.

(Choice D) Most of the laryngeal cartilages develop from the 4th and 6th pharyngeal arches.

(Choice E) The palatine tonsils are derived from the second pharyngeal pouches.

Educational Objective:

Myasthenia gravis is associated with abnormalities of the thymus (e.g. thymoma, thymic hyperplasia). The thymus and inferior parathyroid glands arise from the 3rd pharyngeal pouch.

Embryology Rheumatology/Orthopedics & Sports Myasthenia gravis

Block Time Remaining: 00:42:15

TUTOR

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Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 24-year-old man is brought to the emergency department due to right arm pain after a fall. While rock climbing at a nearby national park, the patient lost his grip and fell approximately 3 m (10 ft) onto the boulders below. He says, "I landed on my right arm and heard something snap." The patient did not strike his head or lose consciousness. He has no chronic medical conditions and takes no daily medications. Vital signs are within normal limits. Physical examination shows extensive bruising over the lateral right arm and a total inability to extend the right wrist. X-ray reveals a midshaft fracture of the right humerus. Which of the following arteries is most likely to be injured in this patient?

- ☐ A. Brachial artery
- ☐ B. Common interosseous artery
- ☐ C. Deep brachial artery
- ☒ D. Posterior circumflex humeral artery
- ☐ E. Radial collateral artery

Submit

Block Time Remaining: 00:42:17

TUTOR

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1



Feedback



Suspend



End Block



A 24-year-old man is brought to the emergency department due to right arm pain after a fall. While rock climbing at a nearby national park, the patient lost his grip and fell approximately 3 m (10 ft) onto the boulders below. He says, "I landed on my right arm and heard something snap." The patient did not strike his head or lose consciousness. He has no chronic medical conditions and takes no daily medications. Vital signs are within normal limits. Physical examination shows extensive bruising over the lateral right arm and a total inability to extend the right wrist. X-ray reveals a midshaft fracture of the right humerus. Which of the following arteries is most likely to be injured in this patient?

- ☐ A. Brachial artery (26%)
- ☐ B. Common interosseous artery (1%)
- ☒ C. Deep brachial artery (47%)
- ☐ D. Posterior circumflex humeral artery (10%)
- ☐ E. Radial collateral artery (13%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



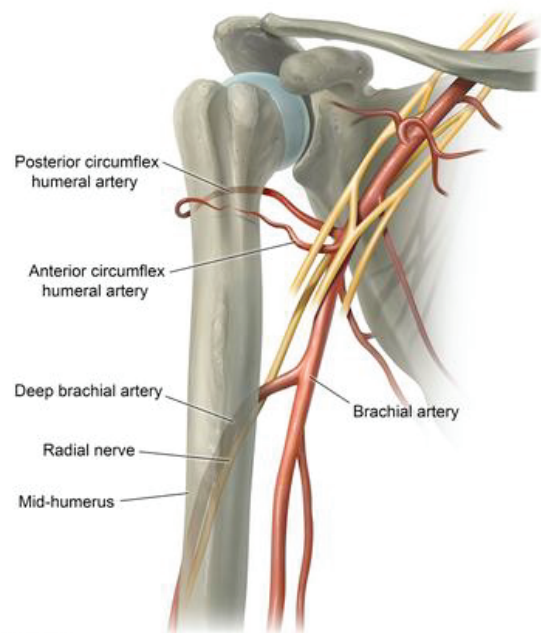
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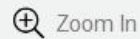
Settings

Exhibit Display

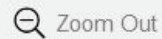
Deep brachial artery & radial nerve



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Zoom Out



Reset



New



Existing



My Notebook

My Notebook



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient has a humerus fracture associated with wrist drop, suggesting a **radial nerve injury**. The radial nerve is a terminal branch of the brachial plexus that carries fibers originating in the C5-T1 nerve roots. It innervates most of the **forearm extensors** at the elbow (eg, triceps) and most of the **hand extensors** at the wrist. It also innervates the extrinsic extensors of the digits and the brachioradialis and supinator muscles. In addition, the radial nerve provides cutaneous sensory innervation to the dorsal hand, forearm, and upper arm.

Radial nerve deficits due to a **midshaft humeral fracture** raise concern for an associated injury to the deep brachial artery. The **deep brachial** (profunda brachii) artery branches off the brachial artery high in the arm, passes inferior to the teres major muscle, and courses posteriorly along the humerus in close association with the radial nerve.

(Choice A) After giving off the deep brachial artery, the brachial artery continues anteromedially until it branches to form the radial and ulnar arteries in the forearm. **Supracondylar fractures** of the humerus may injure the distal portion of the brachial artery but are unlikely to injure the radial nerve or cause wrist drop.

(Choice B) The **common interosseous artery** is a short branch of the ulnar artery that gives rise to anterior, posterior, and recurrent branches within the proximal forearm.

(Choice D) The anterior and posterior circumflex humeral arteries are branches of the axillary artery that



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

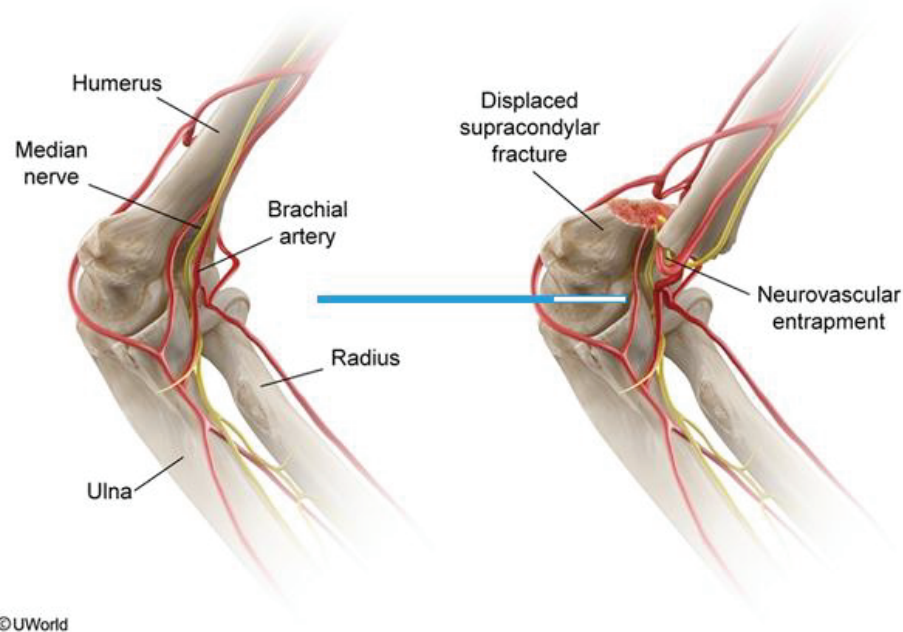
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Text Zoom

Settings

Exhibit Display

Complications of supracondylar fracture



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Zoom Out

Reset

New | Existing

My Notebook



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

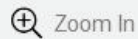
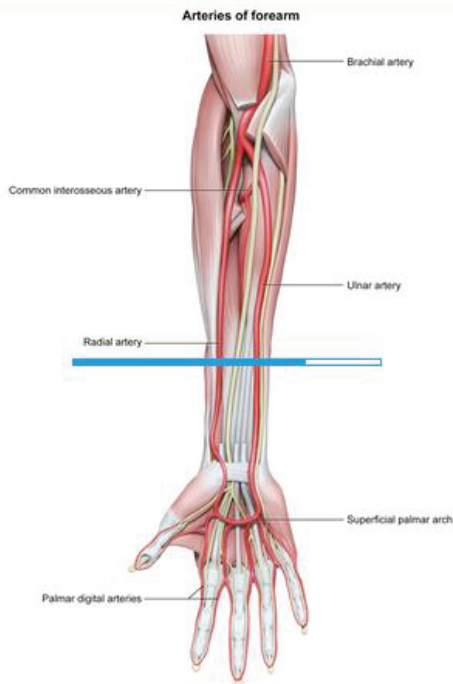


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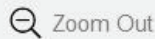


Settings

Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) The **common interosseous artery** is a short branch of the ulnar artery that gives rise to anterior, posterior, and recurrent branches within the proximal forearm.

(Choice D) The anterior and posterior circumflex humeral arteries are branches of the axillary artery that form an anastomosis encircling the surgical neck of the humerus in the **quadrangular space**. The axillary nerve travels in close association with the posterior circumflex artery, and a fracture to the surgical neck of the humerus may damage them.

(Choice E) The deep brachial artery divides into the **radial and middle collateral arteries**. The radial collateral artery also courses with the radial nerve, but injury to this artery from a midshaft fracture is less likely because it originates at the lower end of the spiral groove.

Educational objective:

The deep brachial (profunda brachii) artery and radial nerve run together along the posterior aspect of the humerus. Midshaft fractures of the humerus risk injury to these structures.

Anatomy

Rheumatology/Orthopedics & Sports

Upper extremity long bone fracture

Subject

System

Topic

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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

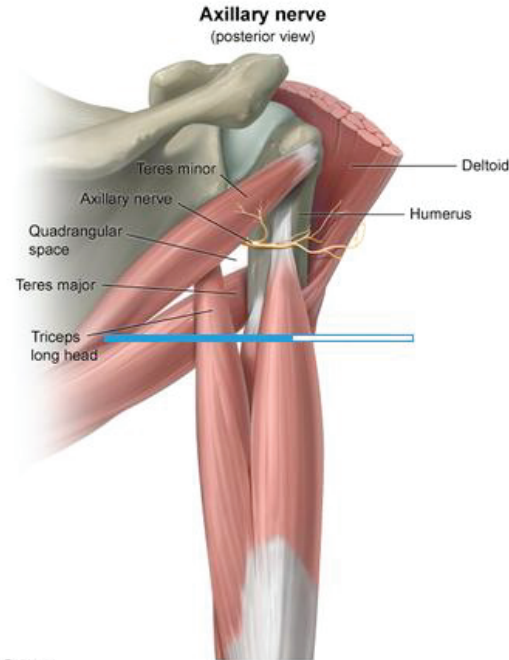
Reverse Color

Text Zoom

Settings

(Choice B) The common interosseous artery is a short branch of the ulnar artery that gives rise to anterior

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Zoom Out

Reset

New | Existing

My Notebook



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

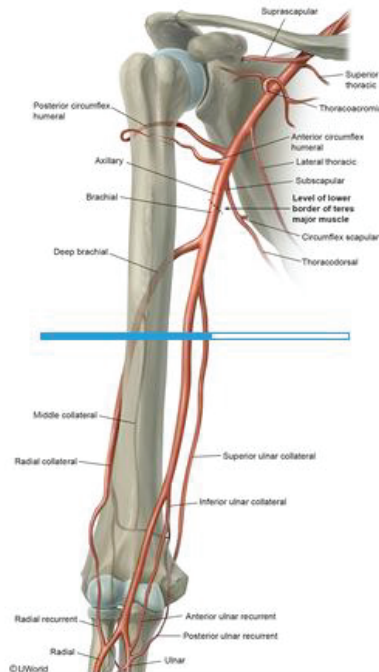
Text Zoom

Settings

(Choice B) The common interosseous artery is a short branch of the ulnar artery that gives rise to anterior

Exhibit Display

Arteries of the upper limb



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Feedback



Suspend



End Block



recently immigrated to the United States and had little access to medical care in her original country. On

physical examination, her proximal interphalangeal and metacarpophalangeal joints are tender and swollen bilaterally, and her fingers appear significantly deformed. Subcutaneous nodules are palpated near the elbow. Laboratory studies are obtained to confirm the diagnosis. This patient's serum is most likely to contain IgM antibodies against which of the following substances?

- ☐ A. Centromeres
- ☐ B. Double-stranded DNA
- ☐ C. Fc portion of human IgG
- ☐ D. Mitochondrial extract
- ☐ E. Nuclear basic proteins
- ☐ F. Phospholipids
- ☐ G. Sheep erythrocytes

Submit



Mark



Previous



Next



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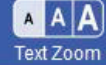
Notes



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Reverse Color



Text Zoom



Settings

A 45-year-old woman comes to the office due to a long history of joint pain, swelling, and stiffness. She recently immigrated to the United States and had little access to medical care in her original country. On physical examination, her proximal interphalangeal and metacarpophalangeal joints are tender and swollen bilaterally, and her fingers appear significantly deformed. Subcutaneous nodules are palpated near the elbow. Laboratory studies are obtained to confirm the diagnosis. This patient's serum is most likely to contain IgM antibodies against which of the following substances?

- ☐ A. Centromeres
- ☐ B. Double-stranded DNA
- ☐ C. Fc portion of human IgG
- ☐ D. Mitochondrial extract
- ☐ E. Nuclear basic proteins
- ☐ F. Phospholipids
- ☐ G. Sheep erythrocytes



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Feedback



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recently immigrated to the United States and had little access to medical care in her original country. On

physical examination, her proximal interphalangeal and metacarpophalangeal joints are tender and swollen bilaterally, and her fingers appear significantly deformed. Subcutaneous nodules are palpated near the elbow. Laboratory studies are obtained to confirm the diagnosis. This patient's serum is most likely to contain IgM antibodies against which of the following substances?

- ☐ A. Centromeres (7%)
- ☐ B. Double-stranded DNA (8%)
- ☒ C. Fc portion of human IgG (67%)
- ☐ D. Mitochondrial extract (2%)
- ☐ E. Nuclear basic proteins (7%)
- ☐ F. Phospholipids (4%)
- ☐ G. Sheep erythrocytes (1%)

Correct

67%
Answered correctly01 min, 44 secs
Time Spent01/11/2021
Last Updated

Block Time Remaining: 00:45:32

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Clinical features of rheumatoid arthritis

Clinical presentation

- Pain, swelling & morning stiffness in multiple joints
- **Small joints** (PIP, MCP, MTP); spares DIP joints
- Systemic symptoms (fever, weight loss, anemia)
- **Cervical spine** involvement: subluxation, cord compression

Laboratory/imaging studies

- Positive rheumatoid factor & **anti-CCP antibodies**
- C-reactive protein & ESR correlate with disease activity
- **X-ray**: soft tissue swelling, joint space narrowing, bony erosions

Anti-CCP = anti-cyclic citrullinated peptide; **DIP** = distal interphalangeal; **ESR** = erythrocyte sedimentation rate; **MCP** = metacarpophalangeal; **MTP** = metatarsophalangeal; **PIP** = proximal interphalangeal.

Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are typical of advanced **rheumatoid arthritis** (RA). Morning stiffness, tenderness, and edema of the affected joints predominate early in this disease. Later, osteopenia, erosions, and joint space narrowing lead to



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are typical of advanced **rheumatoid arthritis** (RA). Morning stiffness, tenderness, and edema of the affected joints predominate early in this disease. Later, osteopenia, erosions, and joint space narrowing lead to decreased range of motion and **deformities** (eg, swan neck, **ulnar deviation**). Patients can also develop **rheumatoid nodules**, firm, nontender, subcutaneous nodules that occur at pressure points such as the elbows or forearms.

RA is due to failure of immune tolerance, with development of an autoreactive immune response directed against joint components (eg, type II collagen, citrullinated vimentin). CD4⁺ T-helper cells become activated by these self-antigens and release cytokines that promote chronic inflammatory synovitis. CD4⁺ T cells also induce B cells to synthesize **rheumatoid factor** and anti-citrullinated protein antibodies (ACPAs). Rheumatoid factor is an antibody (typically IgM) specific for the **Fc component of IgG**. Rheumatoid factor binds circulating IgG and ACPAs bind modified self-proteins, forming immune complexes that deposit on the synovium and cartilage. These complexes activate complement in those locations, contributing to chronic inflammation and joint destruction.

(Choice A) Anticentromere antibodies are found in the majority of patients with **CREST syndrome**.

(Choice B) Antibodies to double-stranded DNA (anti-dsDNA) are specific for systemic lupus



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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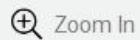
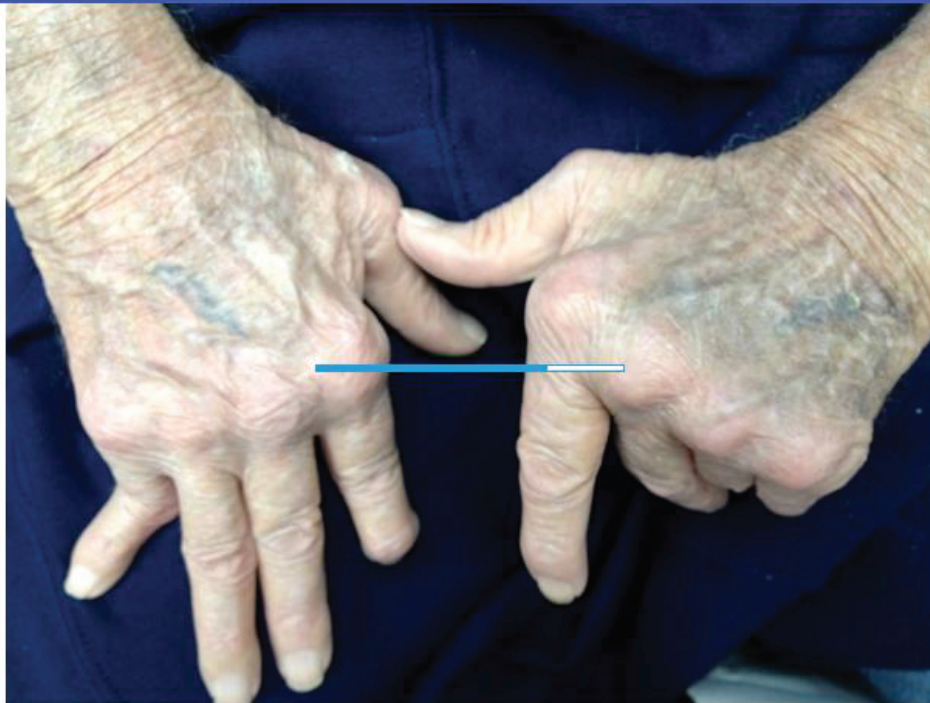
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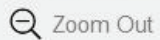
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Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are

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Full Screen



Tutorial



Lab Values



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Calculator



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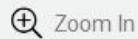
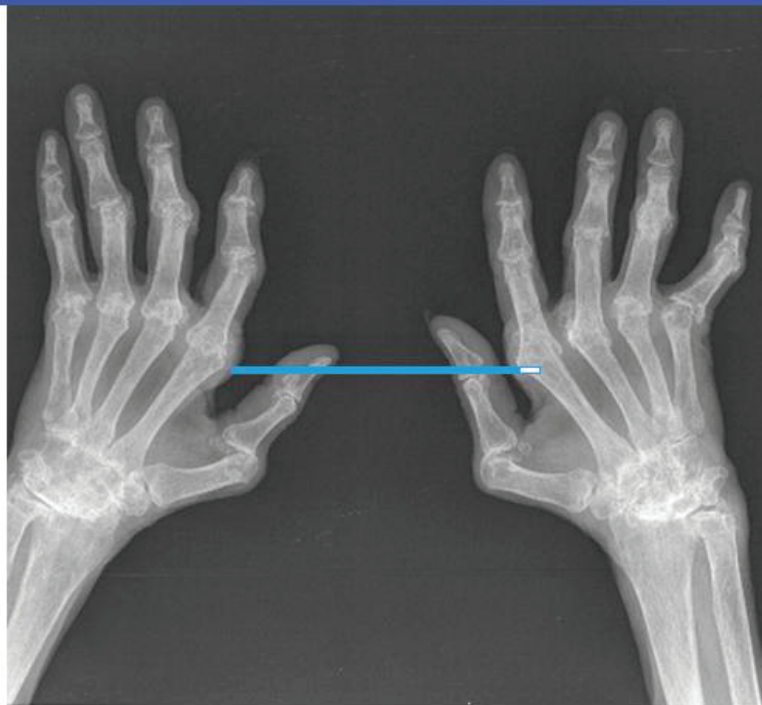
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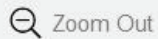
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Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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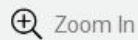
Bilateral pain, stiffness, and deformity of the proximal interphalangeal and metacarpophalangeal joints are

Exhibit Display

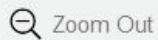
CREST syndrome characteristics

Calcinosis
Raynaud phenomenon
Esophageal dysmotility
Sclerodactyly
Telangiectasias

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice A) Anticentromere antibodies are found in the majority of patients with **CREST syndrome**.

(Choice B) Antibodies to double-stranded DNA (anti-dsDNA) are specific for systemic lupus erythematosus.

(Choice D) Antimitochondrial antibodies are found in patients with primary biliary cholangitis.

(Choice E) The presence of antinuclear antibodies is a nonspecific finding in many connective tissue disorders. These can occur in IgM form, but would be found less frequently than rheumatoid factor in patients with RA.

(Choice F) Antiphospholipid antibodies can be found in patients with systemic lupus erythematosus and antiphospholipid antibody syndrome. Antiphospholipid antibodies cause a hypercoagulable state with paradoxical PTT prolongation.

(Choice G) The Monospot test assesses the serum's ability to agglutinate sheep erythrocytes. It is positive in the presence of heterophile antibodies and is used to diagnose infectious mononucleosis due to Epstein-Barr virus.

Educational objective:

Rheumatoid arthritis results from an immune response directed against autoantigens in the joints.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice D) Antimitochondrial antibodies are found in patients with primary biliary cholangitis.

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(Choice G) The Monospot test assesses the serum's ability to agglutinate sheep erythrocytes. It is positive in the presence of heterophile antibodies and is used to diagnose infectious mononucleosis due to Epstein-Barr virus.

Educational objective:

Rheumatoid arthritis results from an immune response directed against autoantigens in the joints.

Infiltrating CD4⁺ T cells secrete cytokines that promote inflammatory synovitis. They also stimulate B cells to produce rheumatoid factor (IgM antibody specific for Fc component of IgG) and anti-citrullinated protein antibodies that contribute to chronic inflammation and joint destruction.



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Previous



Next



Full Screen



Tutorial



Lab Values



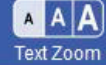
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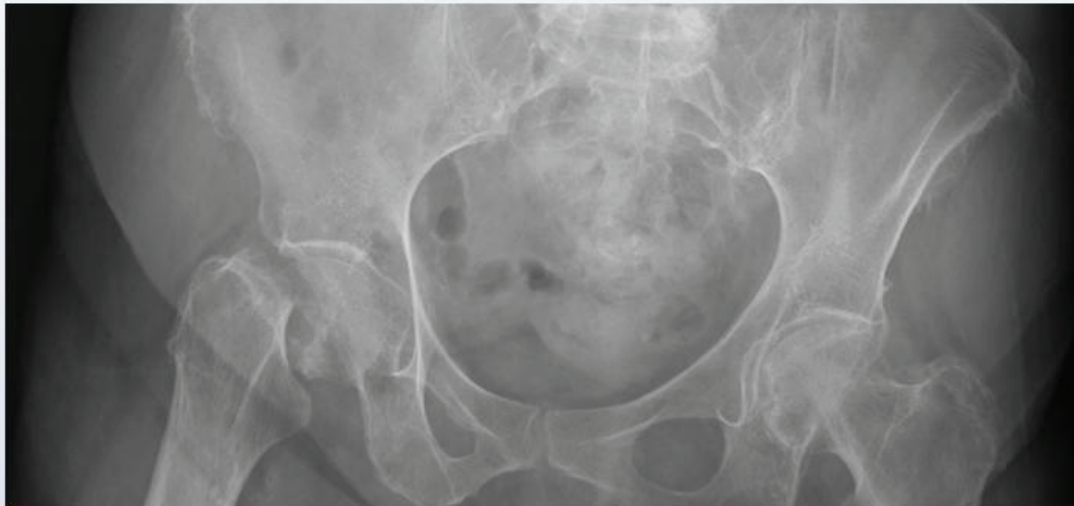


Text Zoom



Settings

A 68-year-old woman is brought to the emergency department with severe right hip pain after a fall. She was walking down a hallway when she tripped on a rug and fell against a wall and then to the floor, landing on her hip. The patient has a history of depression and polymyalgia rheumatica. Current medications include sertraline and low-dose prednisone. She also has a 40-pack-year smoking history. Blood pressure is 145/85 mm Hg and pulse is 96/min. The patient appears to be in significant pain. She is unable to move the right hip, and the right leg appears shorter than the left. A pelvic x-ray is shown in the image below.



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Feedback



Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Injury involving which of the following arteries is most likely to lead to osteonecrosis in this patient?

- ☐ A. Deep femoral
- ☐ B. Inferior gluteal
- ☐ C. Lateral circumflex
- ☐ D. Medial circumflex
- ☐ E. Obturator

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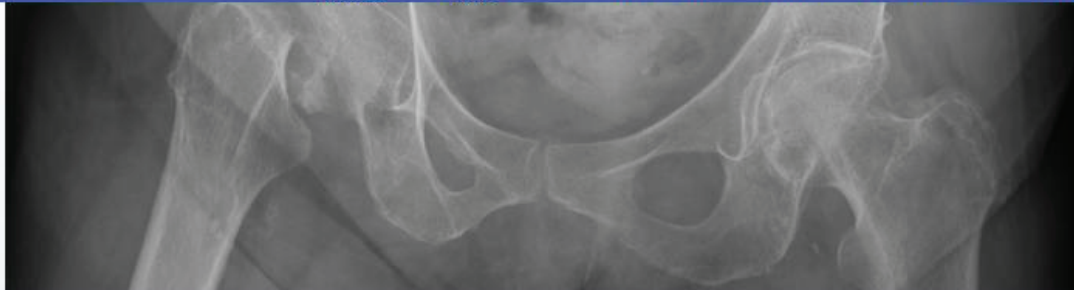
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Injury involving which of the following arteries is most likely to lead to osteonecrosis in this patient?

- ☐ A. Deep femoral (7%)
- ☐ B. Inferior gluteal (2%)
- ☐ C. Lateral circumflex (26%)
- ☒ D. Medial circumflex (57%)
- ☐ E. Obturator (5%)

Correct

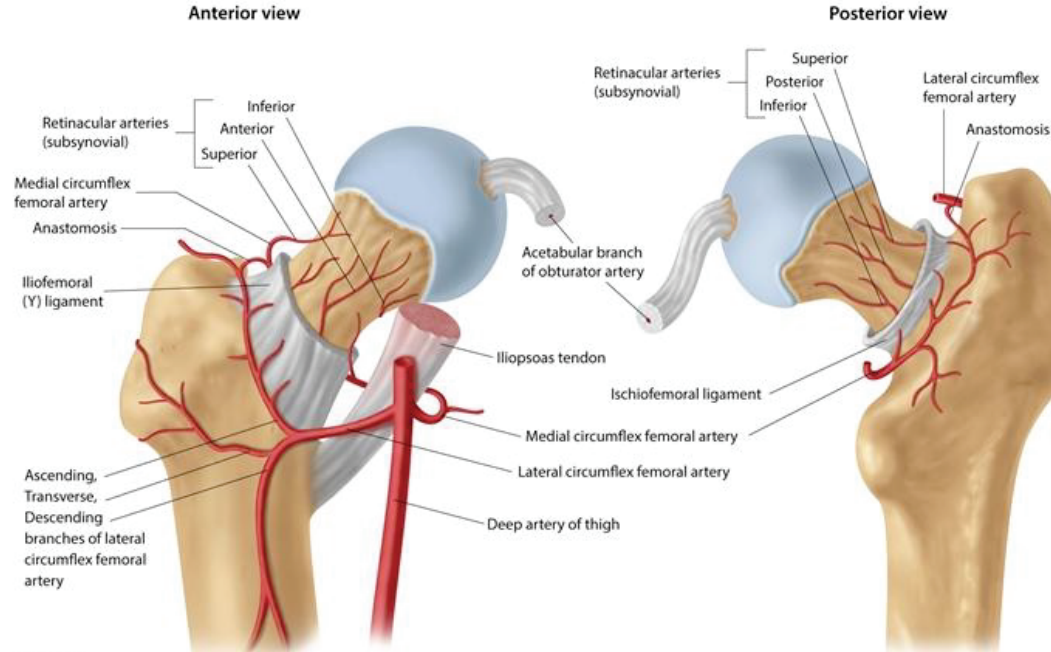
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02/26/2021
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Femoral head arteries



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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This patient's **x-ray** shows a right **femoral neck fracture**, which is common in elderly patients with osteoporosis who have sustained a fall. Femoral neck fractures, especially when displaced, put the femoral head at risk for **osteonecrosis** if its blood supply is disrupted. The blood supply to the femoral head derives mainly from the ascending cervical and retinacular branches of the **medial circumflex artery**. These vessels are especially vulnerable to damage from fractures of the femoral neck due to their close association with it.

(Choice A) The deep femoral artery gives rise to the medial and lateral femoral circumflex arteries. Injury to the femoral artery is less likely as it is more remote from the femoral neck.

(Choices B and C) Branches of the lateral circumflex and superior and inferior gluteal arteries join with the medial circumflex artery to form the trochanteric anastomosis. However, these arteries provide only minor contributions to the blood supply of the femoral head and neck.

(Choice E) The obturator artery gives rise to the artery of the ligamentum teres, which supplies a minor portion of the femoral head. This vessel is important in children because it supplies the region of the femoral head proximal to the epiphyseal growth plate, but it is of minimal clinical significance in adults.

Educational objective:



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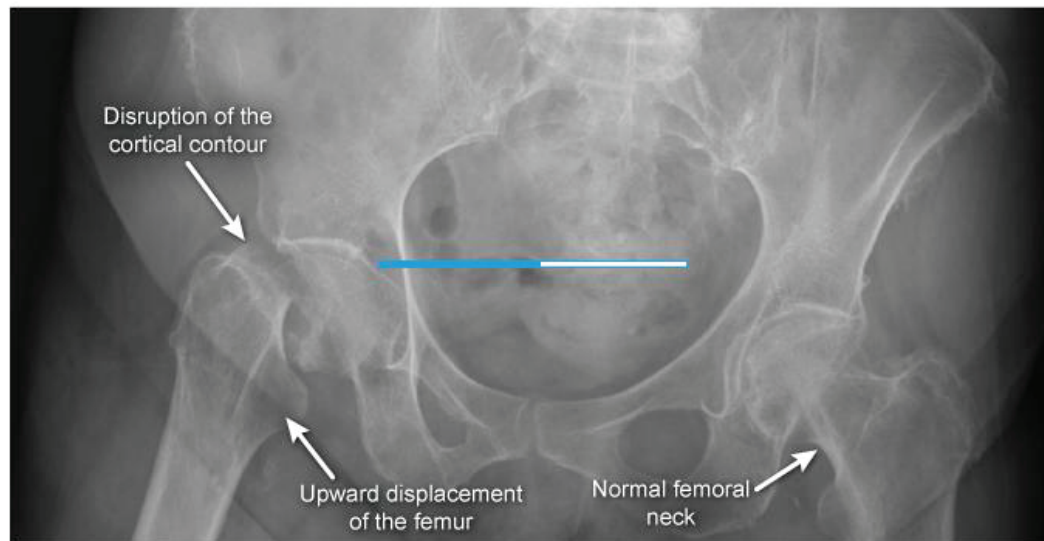
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Exhibit Display

Femoral neck fracture



Zoom In

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My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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Educational objective:

The medial femoral circumflex artery and its branches provide the majority of the blood supply to the femoral head and neck. Injury to these vessels due to a displaced femoral neck fracture can cause osteonecrosis of the femoral head.

References

- [Early prediction of femoral head avascular necrosis following neck fracture.](#)

Anatomy

Rheumatology/Orthopedics & Sports

Lower extremity long bone fracture

Subject

System

Topic



1



Feedback



Suspend



End Block



A 43-year-old man comes to the office due to joint pain and stiffness in both hands for the past 6 months. He sometimes awakens with hand pain at night. Over the last year, the patient also has had chronic fatigue and poor sexual performance. He has no history of serious illness and takes no medications. The patient rarely sees a physician. He does not smoke tobacco or drink alcohol. Blood pressure is 126/80 mm Hg and pulse is 80/min. BMI is 25 kg/m². Hand radiographs reveal bilateral erosions and joint deformities involving the second and third metacarpophalangeal joints. Which of the following is the most likely diagnosis?

- ☐ A. Chronic gouty arthritis
- ☐ B. Hereditary hemochromatosis
- ☐ C. Multiple myeloma
- ☐ D. Reactive arthritis
- ☐ E. Rheumatic fever

Submit



A 43-year-old man comes to the office due to joint pain and stiffness in both hands for the past 6 months. He sometimes awakens with hand pain at night. Over the last year, the patient also has had chronic fatigue and poor sexual performance. He has no history of serious illness and takes no medications. The patient rarely sees a physician. He does not smoke tobacco or drink alcohol. Blood pressure is 126/80 mm Hg and pulse is 80/min. BMI is 25 kg/m². Hand radiographs reveal bilateral erosions and joint deformities involving the second and third metacarpophalangeal joints. Which of the following is the most likely diagnosis?

- ☐ A. Chronic gouty arthritis (19%)
- ✓ ☐ B. Hereditary hemochromatosis (36%)
- ✗ ☒ C. Multiple myeloma (9%)
- ☐ D. Reactive arthritis (28%)
- ☐ E. Rheumatic fever (6%)

Incorrect

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Clinical manifestations of hereditary hemochromatosis

| | |
|-------------------------|--|
| Skin | <ul style="list-style-type: none">• Hyperpigmentation |
| Musculoskeletal | <ul style="list-style-type: none">• Arthritis (particularly 2nd & 3rd MCP joints)• Chondrocalcinosis |
| Gastrointestinal | <ul style="list-style-type: none">• Elevated liver enzymes, hepatomegaly (early)• Cirrhosis & hepatocellular carcinoma (late) |
| Endocrine | <ul style="list-style-type: none">• Diabetes mellitus• Hypopituitarism (eg, secondary hypogonadism, hypothyroidism) |
| Cardiac | <ul style="list-style-type: none">• Restrictive or dilated cardiomyopathy• Conduction abnormalities |

MCP = metacarpophalangeal.

This patient has chronic arthritis, fatigue, and sexual dysfunction, which together suggest **hereditary hemochromatosis (HH)**. HH is an autosomal recessive disease characterized by excessive





This patient has chronic arthritis, fatigue, and sexual dysfunction, which together suggest **hereditary hemochromatosis (HH)**. HH is an autosomal recessive disease characterized by excessive gastrointestinal absorption of **iron**, which is then stored as hemosiderin in various tissues. Manifestations include liver disease, skin hyperpigmentation, diabetes mellitus, pituitary hormone deficiencies (eg, **central hypogonadism**), arthritis, and cardiomyopathy.

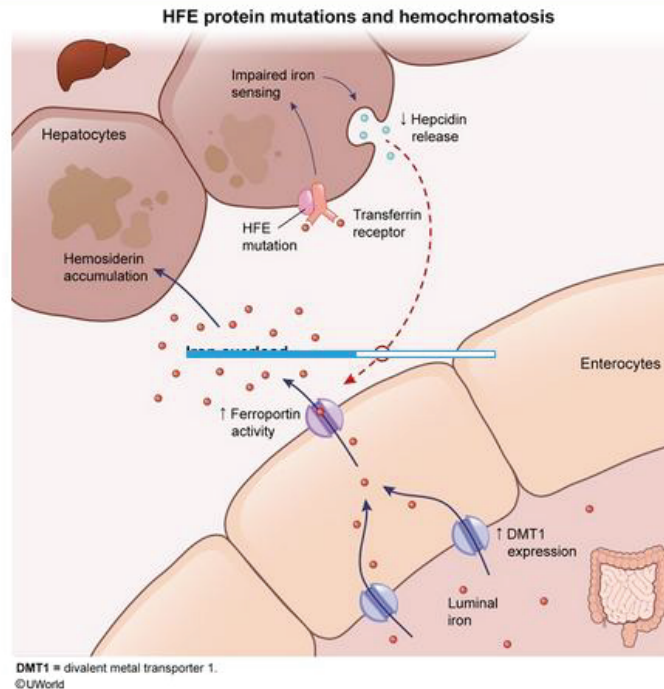
HH-associated arthritis is thought to be caused by **iron deposition** in the articular cartilage and synovium, with subsequent free radical damage and crystal deposition. It typically involves the **second and third metacarpophalangeal (MCP) joints** (in contrast to osteoarthritis of the hands, which most often affects the proximal and distal interphalangeal joints and the first carpometacarpal joint). X-ray findings include characteristic deformities (eg, **hook-like osteophytes**) and deposition of calcium pyrophosphate dihydrate in the articular cartilage (**chondrocalcinosis**).

(Choice A) Gouty arthritis may occasionally present as a chronic arthritis of the small joints of the hands and feet, superficially resembling rheumatoid arthritis. X-ray often shows associated **bony erosions**. However, most patients have a history of acute gout attacks, and gout would not explain this patient's fatigue and sexual dysfunction.

(Choice C) Multiple myeloma usually occurs in older patients and is rare at age <50. Characteristic x-ray



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(Choice C) Multiple myeloma usually occurs in older patients and is rare at age <50. Characteristic X-ray

Block Time Remaining: 00:02:49

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Feedback

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15

16

17

18

19

20

21

22

23

24

25

26

27

Item 1 of 40

Question Id: 15663

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display

Hereditary hemochromatosis



Hook-like osteophyte

Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:02:49

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



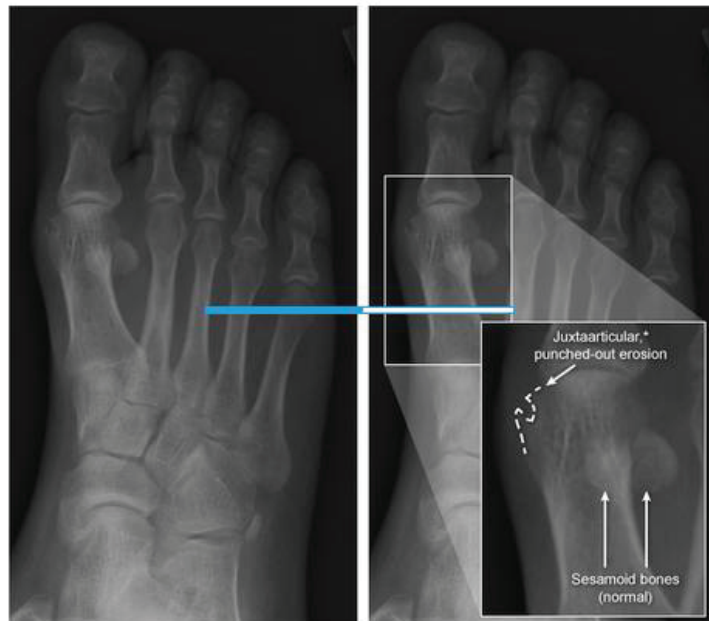
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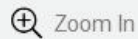
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Gout

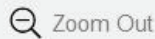


*Erosions are commonly near (but not at) the articular surface

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(Choice C) Multiple myeloma usually occurs in older patients and is rare at age <50. Characteristic X-ray

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(Choice C) Multiple myeloma usually occurs in older patients and is rare at age <50. Characteristic x-ray findings include scattered osteolytic lesions that typically involve the axial skeleton.

(Choice D) Reactive arthritis typically presents with asymmetric oligoarthritis, enthesitis (ie, inflammation at tendon/ligament insertion sites), and dactylitis (ie, sausage digit). It is often associated with extraarticular symptoms, including conjunctivitis, uveitis, and urethritis. Symptoms usually resolve within a few months and would not be chronic.

(Choice E) Rheumatic fever is an immune-mediated complication of streptococcal infections characterized by migratory arthritis, carditis, subcutaneous nodules, rash (erythema marginatum), and chorea. It is most common at age 5-15 and presents acutely 2-4 weeks after an episode of untreated pharyngitis.

Educational objective:

Hereditary hemochromatosis is an autosomal recessive disease characterized by excessive gastrointestinal absorption of iron, which is then stored as hemosiderin in various tissues. Secondary arthritis is common and typically involves the second and third metacarpophalangeal joints. Other manifestations include liver disease, skin hyperpigmentation, diabetes mellitus, pituitary hormone deficiencies (eg, central hypogonadism), and cardiomyopathy.



A 54-year-old man comes to the office due to aching pain in his left neck and shoulder area for the past several months. He has also had numbness and weakness of the left hand. The patient recalls no major trauma and has no prior medical problems. He tried chiropractic and massage therapies, but the symptoms persisted. Left upper extremity examination shows decreased sensation in the palm and index and middle fingers along with weakness of left wrist extension. The left biceps and brachioradialis deep tendon reflexes are normal, but the triceps reflex is diminished. Right upper extremity examination is normal. A lesion affecting which of the following labeled sections of the brachial plexus is the most likely cause of this patient's neurologic findings?

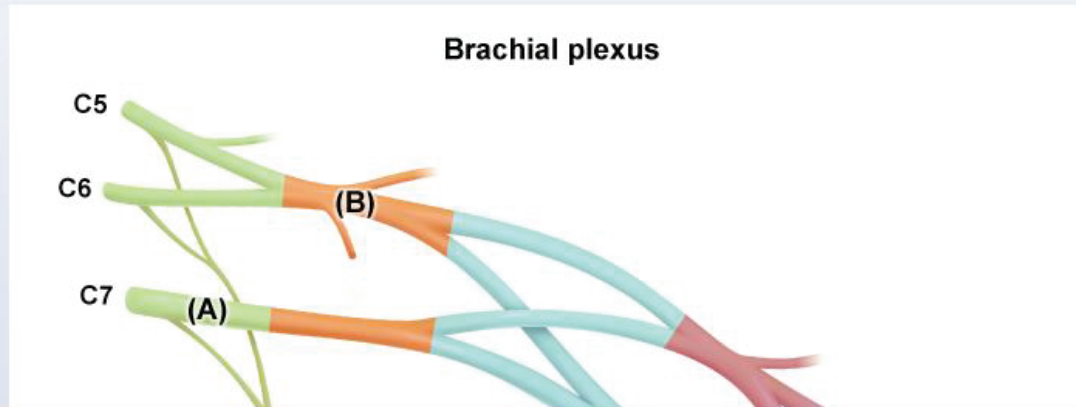
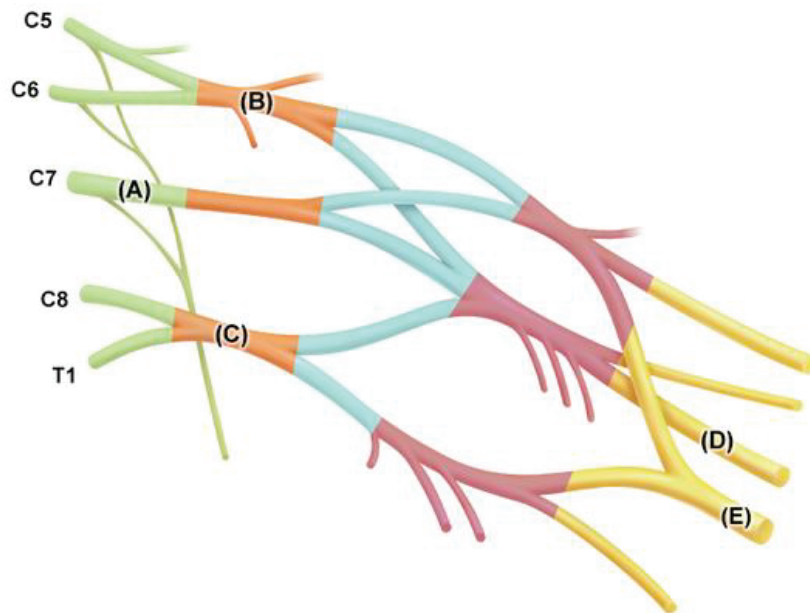


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Brachial plexus



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My Notebook

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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit

T1

(D)

(E)

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- ✓ ☒ A.A (38%)
- ☐ B.B (8%)
- ☐ C.C (14%)
- ☐ D.D (30%)
- ☐ E.E (8%)

Correct

38%

01 min, 16 secs

12/03/2020

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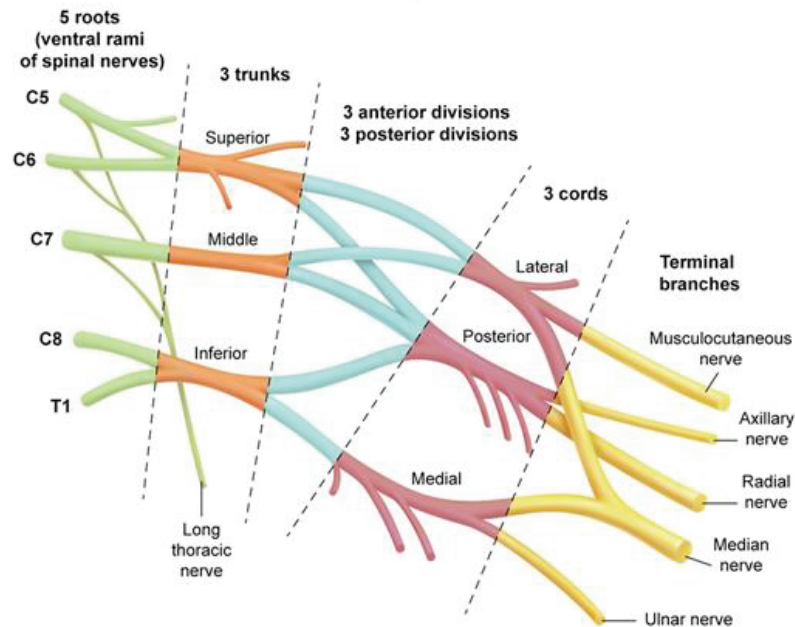
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5 roots

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Brachial plexus



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Ulnar nerve

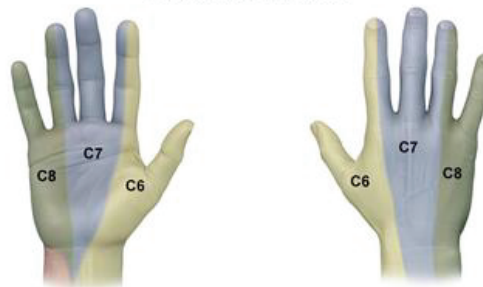
The C5 through T1 nerve roots form the brachial plexus trunks, divisions, cords, and ultimately terminal branches, which supply sensory and motor innervation to the upper extremities. This patient has deficits involving both the **radial** (eg, triceps reflex, wrist extension) and **median** (sensation to **palm and index and middle finger**) nerves. This pattern of deficits across **multiple peripheral nerves** indicates a lesion **proximal** to the formation of the terminal branches.

In a patient without history of trauma or malignancy, chronic shoulder and **radicular arm pain** with sensorimotor deficits is most likely caused by compression of a nerve root due to **cervical spondylosis**. The **C7 root** is the most frequently affected nerve root in patients with cervical radiculopathy, resulting in deficits across the median and radial nerve distributions.

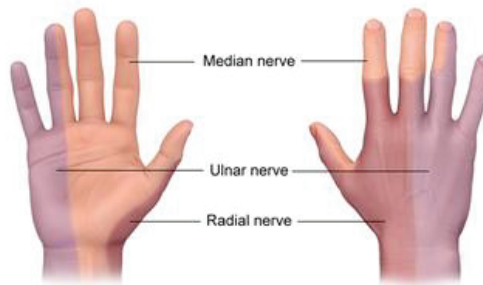
(Choices B and C) Damage to the superior or inferior trunk most often occurs as a result of trauma (eg, traction during delivery in infants; falls in adults). A superior trunk lesion (eg, Erb-Duchenne palsy) would result in loss of arm abduction, elbow flexion, and wrist extension (**waiter's tip** position: adducted arm with extended elbow and flexed wrist). An inferior trunk lesion (eg, Klumpke palsy) typically results in loss of wrist/metacarpophalangeal joint flexion and interphalangeal joint extension (**claw hand** position: extended wrist/metacarpophalangeal joints with flexed interphalangeal joints).

Exhibit Display

Dermatomes of the hand



Cutaneous innervation of the hand



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Features of cervical radiculopathy

| Nerve root (Disc space) | Reflex affected | Sensory loss* | Weakness |
|----------------------------|-------------------------------|-------------------------------------|---|
| C5 (C4-5) | • Biceps | • Lateral upper arm | • Shoulder abduction (deltoid) • Elbow flexion (biceps) |
| C6 (C5-6) | • Biceps • Brachioradialis | • Thumb • Index finger | • Elbow flexion (biceps) • Forearm pronation/supination (brachioradialis) • Wrist extension |
| C7 (C6-7) | • Triceps | • Dorsal forearm • Middle finger | • Elbow extension (triceps) • Wrist flexion • Finger extension |
| C8 (C7-T1) | • Finger flexors** | • Ring & little fingers | • Finger flexion & extension • Thumb flexion & abduction |
| T1 (T1-2) | • Finger flexors** | • Medial forearm | • Finger abduction & adduction |

*In addition to neck/shoulder pain, radicular pain typically has a similar distribution to sensory loss.

**Not typically evaluated clinically.

⚡ New | Existing

The C5 through T1 branches, which supply the middle finger) nerve

proximal to the for

In a patient without sensorimotor deficit

The C7 root is the most common deficit across the

(Choices B and C)

traction during delivery

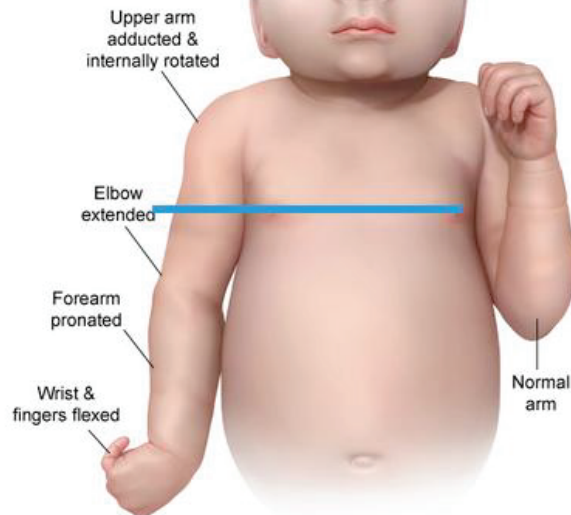
result in loss of arm

extended elbow and

wrist/metacarpophalangeal

extended wrist/metacarpophalangeal

Exhibit Display

Erb-Duchenne palsy
"Waiter tip"

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Klumpke palsy
"Claw hand"Metacarpophalangeal
joints hyperextendedWrist
extendedInterphalangeal
joints flexedForearm
supinatedNormal
arm

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My Notebook

extended elbow and flexed wrist). An inferior trunk lesion (eg, Klumpke palsy) typically results in loss of wrist/metacarpophalangeal joint flexion and interphalangeal joint extension (**claw hand** position: extended wrist/metacarpophalangeal joints with flexed interphalangeal joints).

(Choices D and E) Damage to one of the terminal branches of the brachial plexus would result in a pattern of deficits restricted to the sensory and/or motor function of one nerve. The radial nerve can be injured by compression against the humerus (eg, Saturday night palsy) or by a humerus fracture, causing weakness in wrist extension (eg, wrist drop). Injury to the median nerve most commonly occurs at the wrist (eg, carpal tunnel syndrome) with resulting numbness, tingling, and pain in the palm and first 3 digits.

Educational objective:

Motor and sensory deficits across multiple peripheral upper extremity nerves (eg, radial and median) indicate a lesion in the brachial plexus proximal to the formation of the terminal branches. In the absence of history of trauma or malignancy, the most likely cause is nerve root compression due to cervical spondylosis (cervical radiculopathy).

References

- [Diagnosis and treatment of cervical radiculopathy and myelopathy.](#)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 72-year-old woman comes to the office due to persistent headaches, fatigue, and muscle pain. She has a history of hypertension and osteoarthritis. The patient does not use tobacco, alcohol, or illicit drugs. Her father had a subarachnoid hemorrhage from a ruptured berry aneurysm. She is treated with prednisone, leading to marked and rapid improvement in her symptoms. Which of the following pathologic processes is most likely responsible for this patient's condition?

- ☐ A. Granulomatous inflammation of the media
- ☐ B. Homogenous acellular thickening of arteriolar walls
- ☐ C. Medial band-like calcifications
- ☐ D. Onion-like concentric thickening of arteriolar walls
- ☐ E. Transmural inflammation with fibrinoid necrosis

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Mark



Previous



Next



Full Screen



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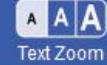
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 72-year-old woman comes to the office due to persistent headaches, fatigue, and muscle pain. She has a history of hypertension and osteoarthritis. The patient does not use tobacco, alcohol, or illicit drugs. Her father had a subarachnoid hemorrhage from a ruptured berry aneurysm. She is treated with prednisone, leading to marked and rapid improvement in her symptoms. Which of the following pathologic processes is most likely responsible for this patient's condition?

- ☒ A. Granulomatous inflammation of the media (65%)
- ☐ B. Homogenous acellular thickening of arteriolar walls (4%)
- ☐ C. Medial band-like calcifications (1%)
- ☐ D. Onion-like concentric thickening of arteriolar walls (8%)
- ☐ E. Transmural inflammation with fibrinoid necrosis (20%)

Correct

 65%
Answered correctly 59 secs
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Last Updated

Block Time Remaining: 00:05:04

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Mark



Previous



Next



Full Screen



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Lab Values



Notes



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Settings

Giant cell arteritis

| | |
|------------------|--|
| Symptoms | <ul style="list-style-type: none">• Systemic: fever, fatigue, malaise, weight loss• Headache• Jaw claudication• Visual disturbances (eg, ischemic optic neuropathy)• Polymyalgia rheumatica |
| Diagnosis | <ul style="list-style-type: none">• Elevated erythrocyte sedimentation rate & C-reactive protein• Temporal artery biopsy: intimal thickening, elastic lamina fragmentation, multinucleated giant cells |
| Treatment | <ul style="list-style-type: none">• Glucocorticoids |

This patient, an elderly woman with headaches, muscular pain, and a **rapid response to glucocorticoids**, has typical features of **giant cell arteritis (GCA)**. GCA is the most common form of vasculitis in persons of northern European descent and occurs almost exclusively in patients **age >50**. About half of patients with GCA will also have **polymyalgia rheumatica**, which causes achy pain in the shoulder and hip girdles.



1



Feedback



Suspend



End Block

GCA will also have **polymyalgia rheumatica**, which causes achy pain in the shoulder and hip girdles.

GCA also confers a higher risk of thoracic aortic aneurysms, but not berry aneurysms (her father's history is likely unrelated to her presentation).

GCA is characterized by a T-cell-mediated inflammatory process of medium-to-large arteries. It may occur diffusely but predominantly affects the arteries of the head and neck, especially the **temporal artery** (ie, temporal arteritis). Biopsy of the temporal artery will show scattered, focal **granulomatous inflammation** (most pronounced in the **media**) with **intimal thickening**, **elastic lamina fragmentation**, and **giant cell formation** (without distinct granulomas). GCA is histologically identical to Takayasu arteritis, which typically involves the aortic arch and affects primarily younger patients.

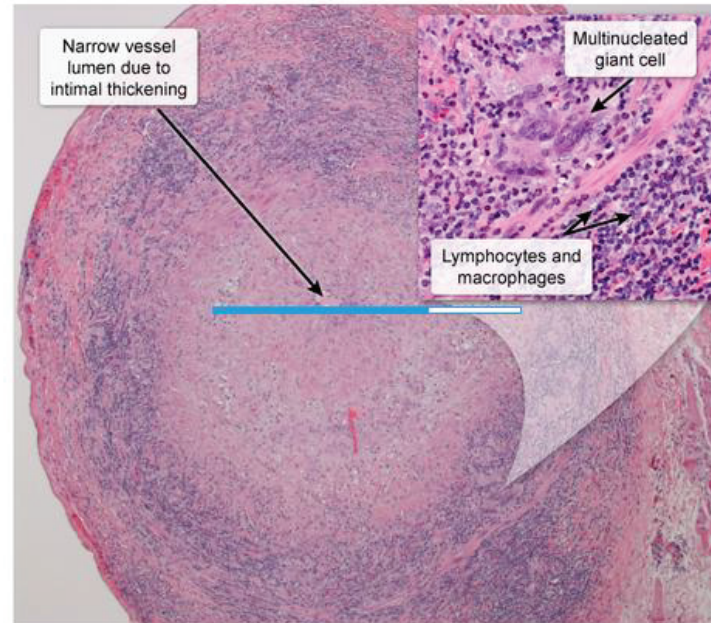
(Choices B and D) **Hyaline arteriosclerosis** is characterized by deposition of homogeneous hyaline material in the intima and media of small arteries and arterioles. It is associated with diabetes, hypertension, and advanced age. Severe hypertension also results in **hyperplastic arteriosclerosis**, which manifests as onion-like concentric thickening of the walls of arterioles (eg, laminated smooth muscle cells, reduplicated basement membranes). Both forms of arteriosclerosis can cause end-organ ischemic injury. However, the resulting symptoms/signs would not respond to glucocorticoids.

(Choice C) Medial band-like calcifications are characteristic of Mönckeberg's medial calcific sclerosis and present as pipestem calcifications on x-ray. They may be associated with atherosclerosis but do not

GCA will also have **polymyalgia rheumatica**, which causes aching pain in the shoulder and hip girdles.

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Giant cell arteritis



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present as osteopenic calcifications on x-ray. They may be associated with atherosclerosis but do not

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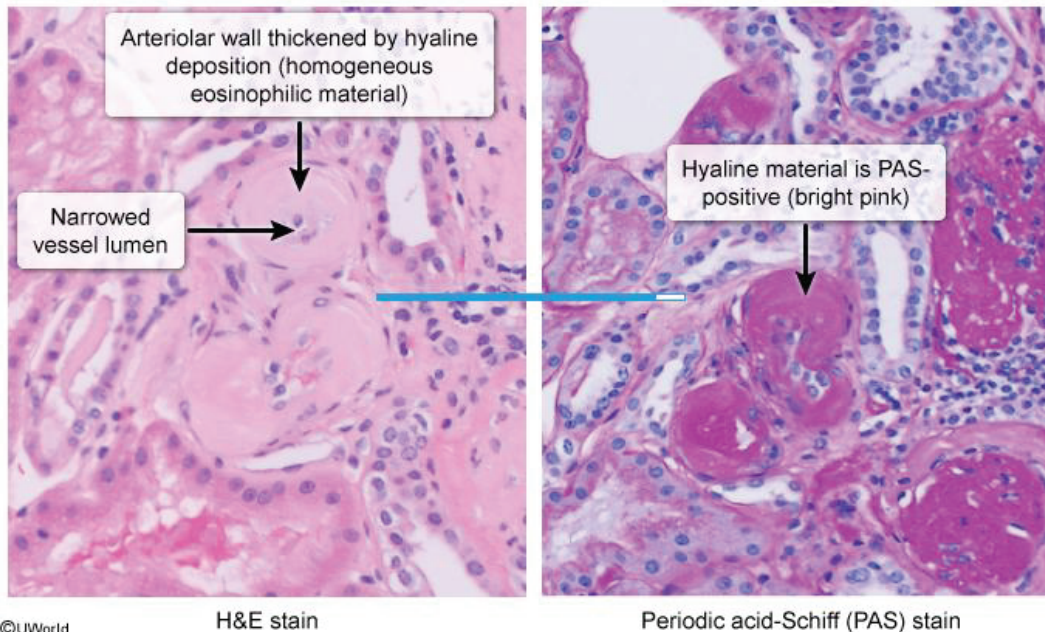
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GCA will also have **polymyalgia rheumatica**, which causes aches in the shoulder and hip girdles.

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Hyaline arteriolosclerosis



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present as osteopenic calcifications on x-ray. They may be associated with atherosclerosis but do not

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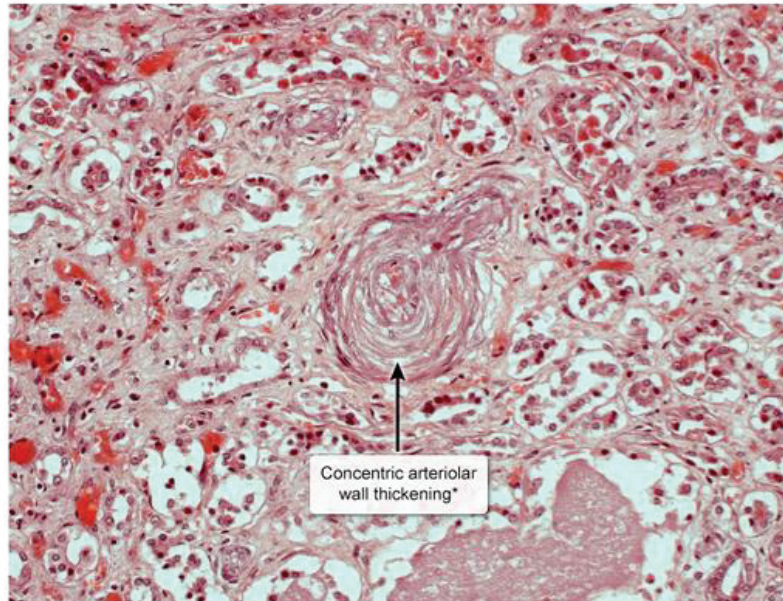
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GCA will also have **polymyalgia rheumatica**, which causes aches in the shoulder and hip girdles.

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Hyperplastic arteriolosclerosis



**Onion skin" appearance

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My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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injury. However, the resulting symptoms/signs would not respond to glucocorticoids.

(Choice C) Medial band-like calcifications are characteristic of Mönckeberg's medial calcific sclerosis and present as pipestem calcifications on x-ray. They may be associated with atherosclerosis but do not directly cause symptoms and are usually not clinically significant.

(Choice E) Transmural inflammation of the arterial wall with fibrinoid necrosis is consistent with [polyarteritis nodosa](#). This uncommon form of vasculitis typically occurs in young adults and presents with intermittent episodes of a variety of manifestations, including abdominal pain, peripheral neuropathy, renal insufficiency, and severe hypertension.

Educational objective:

Giant cell arteritis is characterized by granulomatous inflammation of the media with intimal thickening and predominantly involves branches of the carotid artery, especially the temporal artery. It is strongly associated with polymyalgia rheumatica; both conditions respond promptly to glucocorticoid therapy.

Pathology

Rheumatology/Orthopedics & Sports

Giant cell arteritis

Subject

System

Topic

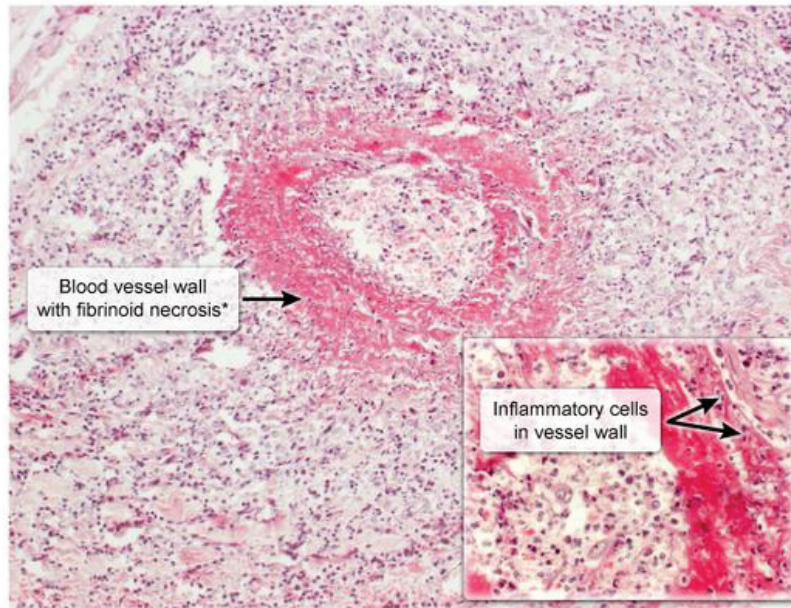
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injury. However the resulting symptoms/signs would not respond to glucocorticoids

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Polyarteritis nodosa



*Eosinophilic fibrin deposits in vessel wall.

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A 38-year-old man comes to the office due to pain in multiple joints. He has a 5-year history of lumbar pain and a 2-year history of bilateral knee pain. The patient works in construction and his pain is worst after a long day on his feet. He has taken ibuprofen intermittently, but the pain is no longer tolerable. The patient has a paternal aunt with osteoarthritis. Physical examination shows blue-black spots on his sclerae and diffuse darkening of the auricular helices. Which of the following is the most likely cause of this patient's arthritis?

- ☐ A. Homogentisic acid dioxygenase deficiency
- ☐ B. Hyperuricemia
- ☐ C. Multifactorial articular cartilage failure
- ☐ D. Recent infection with *Salmonella*
- ☐ E. Tyrosinase deficiency

Submit

A 38-year-old man comes to the office due to pain in multiple joints. He has a 5-year history of lumbar pain and a 2-year history of bilateral knee pain. The patient works in construction and his pain is worst after a long day on his feet. He has taken ibuprofen intermittently, but the pain is no longer tolerable. The patient has a paternal aunt with osteoarthritis. Physical examination shows blue-black spots on his sclerae and diffuse darkening of the auricular helices. Which of the following is the most likely cause of this patient's arthritis?

- ✓ ☒ A. Homogentisic acid dioxygenase deficiency (69%)
- ☐ B. Hyperuricemia (3%)
- ☐ C. Multifactorial articular cartilage failure (18%)
- ☐ D. Recent infection with *Salmonella* (0%)
- ☐ E. Tyrosinase deficiency (6%)

Correct

69%
Answered correctly

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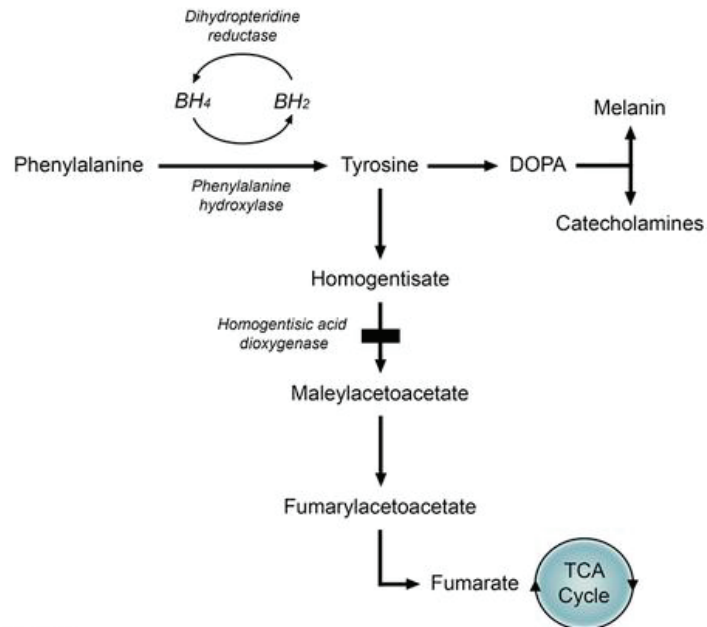
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Alkaptonuria



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Alkaptonuria is a relatively benign childhood disorder that is marked by severe **arthritis** in adult life. This **autosomal-recessive** disorder is caused by **deficiency of homogentisic acid dioxygenase**, which normally metabolizes homogentisic acid into maleylacetoacetate. Accumulated homogentisic acid causes pigment deposits in **connective tissue** throughout the body. During adulthood, these **blue-black deposits** become apparent in the sclerae and ear cartilage. Deposits also occur in the large joints and spine, causing ankylosis, motion restriction, and significant pain. A distinctive characteristic of alkaptonuria is that the urine of these patients turns black when exposed to air due to oxidization of homogentisic acid.

(Choice B) Hyperuricemia can cause acute monoarticular gouty arthritis due to urate crystal deposition in joints (usually the great toe or knee). These acute attacks resolve in days to weeks and are not associated with connective tissue hyperpigmentation.

(Choice C) Osteoarthritis is due to combined genetic, metabolic, and mechanical factors that result in defects in articular cartilage. Polyarticular joint involvement of the fingers (including **Heberden** and Bouchard nodes), knees, hips, and spine classically occur. Joint pain typically peaks in the afternoon or evening after activity, but osteoarthritis is not associated with the blue-black deposits.

(Choice D) Reactive arthritis can occur following enteric or genitourinary infections with organisms such as

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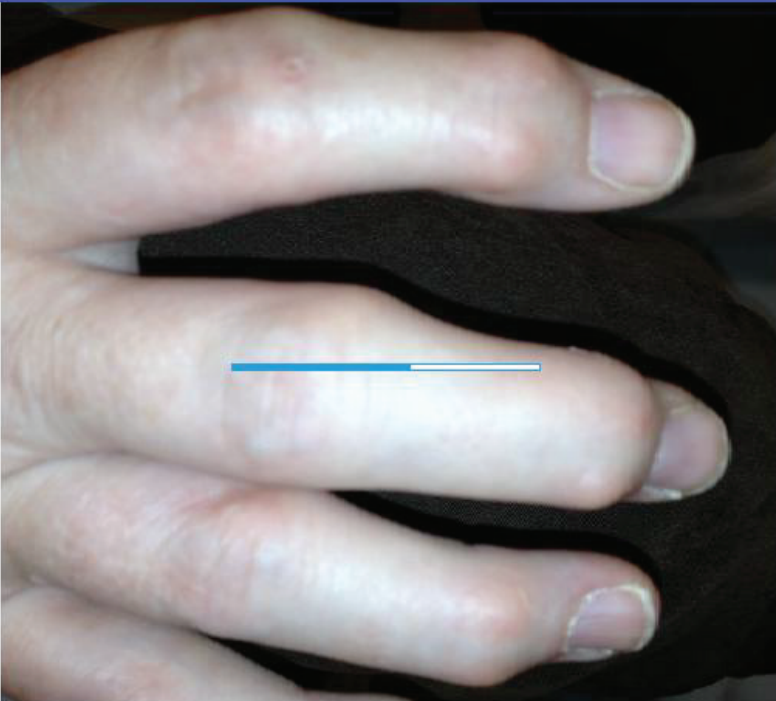
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
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Exhibit Display



 Zoom In  Zoom Out  Reset  New | Existing  My Notebook

evening after activity, but osteoarthritis is not associated with the blue-black deposits.

(Choice D) Reactive arthritis can occur following enteric or genitourinary infections with organisms such as *Salmonella*, *Shigella*, *Campylobacter*, and *Chlamydia*. The typical pattern is asymmetric involvement of lower extremity joints accompanied by enthesitis (inflammation at insertion of tendons), conjunctivitis, and urethritis. Reactive arthritis has no associated skin findings in contrast to alkaptonuria.

(Choice E) Albinism is caused by defects in biosynthesis and distribution of melanin. Melanocytes synthesize melanin from tyrosine via the enzyme tyrosinase.

Educational objective:

Alkaptonuria is an autosomal-recessive disorder caused by a deficiency of homogentisic acid dioxygenase, an enzyme involved in tyrosine metabolism. Excess homogentisic acid causes diffuse blue-black deposits in connective tissues. Adults have sclerae and ear cartilage hyperpigmentation along with osteoarthropathy of the spine and large joints.

References

- [Alkaptonuria.](#)
- [Alkaptonuria.](#)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

A 17-year-old boy is referred to a clinic for ongoing muscle weakness. He has noticed difficulty climbing stairs at home over the last several months, and he recently stopped playing basketball due to difficulty lifting the ball over his head. The patient takes no medications and does not know of any family members with muscle weakness. On neurologic examination, he is unable to lift his arms or legs against resistance when fully outstretched. He undergoes a muscle biopsy to evaluate the cause of his proximal muscle weakness. Electron microscopy of the specimen reveals sparse transverse tubules in some of the muscle fibers. Which of the following is the most likely consequence of this patient's biopsy findings?

- ☐ A. Decremental force generation on repeated muscle stimulation
- ☐ B. Impaired ATP production during active muscle contraction
- ☐ C. Impaired relaxation after sustained muscle contraction
- ☐ D. No contraction of the myocyte in response to increased intracellular Ca^{2+}
- ☐ E. Uncoordinated contraction of myofibrils within affected muscle fibers

Submit

Block Time Remaining: 00:06:48

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A 17-year-old boy is referred to a clinic for ongoing muscle weakness. He has noticed difficulty climbing stairs at home over the last several months, and he recently stopped playing basketball due to difficulty lifting the ball over his head. The patient takes no medications and does not know of any family members with muscle weakness. On neurologic examination, he is unable to lift his arms or legs against resistance when fully outstretched. He undergoes a muscle biopsy to evaluate the cause of his proximal muscle weakness. Electron microscopy of the specimen reveals **sparse transverse tubules** in some of the muscle fibers. Which of the following is the most likely consequence of this patient's biopsy findings?

- ☐ A. Decremental force generation on repeated muscle stimulation (13%)
- ☐ B. Impaired ATP production during active muscle contraction (8%)
- ☐ C. Impaired relaxation after sustained muscle contraction (3%)
- ☐ D. No contraction of the myocyte in response to increased intracellular Ca^{2+} (21%)
- ☒ E. Uncoordinated contraction of myofibrils within affected muscle fibers (52%)





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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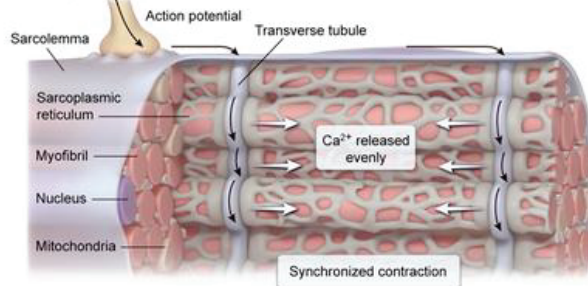


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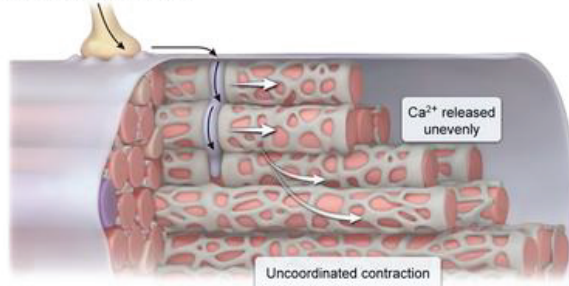
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Muscle fiber depolarization

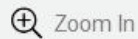
Healthy muscle cell



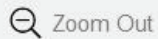
Fewer transverse tubules



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Transverse tubules (T-tubules) are **invaginations** of the muscle cell membrane (**sarcolemma**) located in close proximity to the terminal cisterns of the sarcoplasmic reticulum. They are found in striated (eg, cardiac, skeletal) muscle and contain voltage-gated L-type calcium channels (dihydropyridine receptors) adjacent to the ryanodine receptors on the terminal cisterns. During muscle contraction, T-tubules allow the **depolarization** impulse to **rapidly propagate** through the interior of the muscle fiber. This ensures that **calcium release** from the sarcoplasmic reticulum occurs uniformly throughout the fiber, allowing for **synchronized contraction of myofibrils** in each muscle cell.

This patient most likely has a form of limb girdle muscular dystrophy due to a mutated sarcolemma protein (eg, caveolin) affecting excitation-contraction coupling. Decreased numbers of functional T-tubules in affected muscle fibers lead to **uncoordinated** contraction of myofibrils, which manifests as muscle weakness.

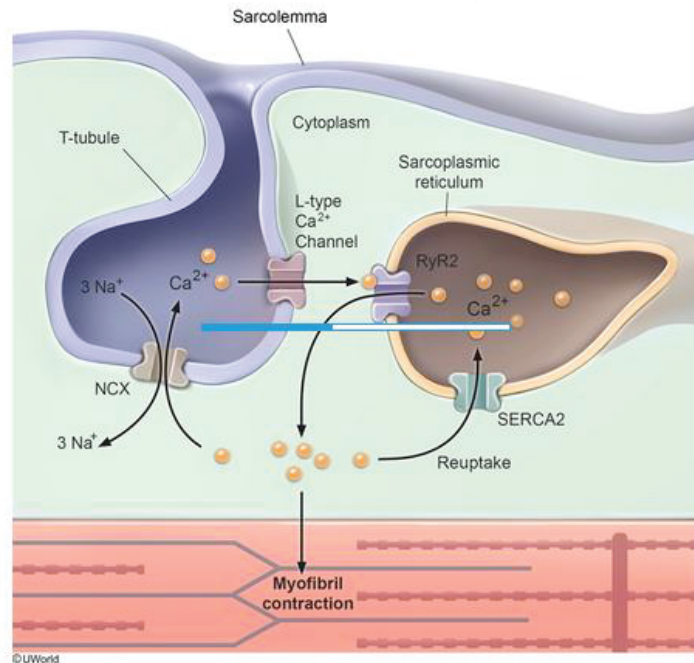
(Choice A) Decremental force generated on repeated stimulation characterizes myasthenia gravis, an autoantibody disorder inhibiting postsynaptic acetylcholine receptors in the neuromuscular junction. A constant low response to repeated nerve stimulation is more likely if T-tubules are lacking.

(Choice B) ATP fuels myosin movement along actin filaments (causing contraction) and drives the pumps that transport calcium back into the sarcoplasmic reticulum (causing relaxation). McArdle disease is one



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Intracellular calcium regulation



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Reset

New | Existing

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(Choice B) ATP fuels myosin movement along actin filaments (causing contraction) and drives the pumps that transport calcium back into the sarcoplasmic reticulum (causing relaxation). McArdle disease is one cause of impaired ATP production and occurs due to a failure of muscle glycogen breakdown.

(Choice C) Impaired relaxation after sustained contraction occurs in myotonic dystrophy due to a trinucleotide repeat expansion altering myotonin-protein kinase. This protein facilitates myosin head detachment from the actin filament to enable muscle relaxation; T-tubules do not play a role.

(Choice D) A mutation in **troponin C** may block its response to intracellular calcium and prevent muscle contraction. However, muscle fibers with decreased numbers of T-tubules will maintain limited contractility.

Educational objective:

Transverse tubules (T-tubules) are invaginations of the sarcolemma that transmit depolarization signals to the sarcoplasmic reticulum to trigger the release of calcium and induce muscle contraction. The uniform distribution of T-tubules in striated muscle fibers ensures that each myofibril contracts at the same time, which is necessary for efficient contraction.

References

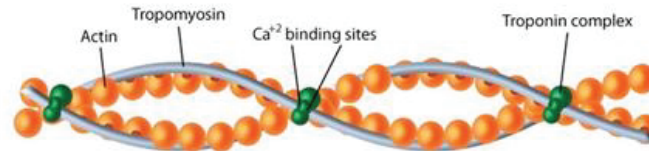
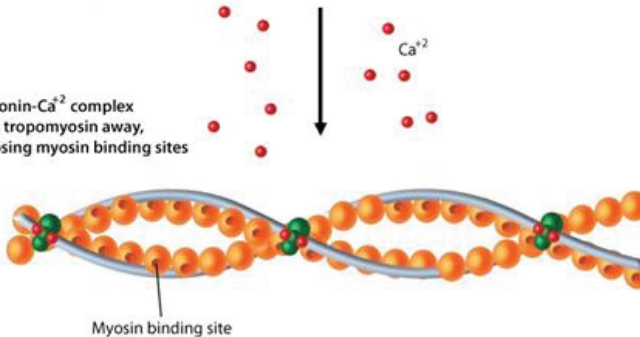
- T-tubule biogenesis and triad formation in skeletal muscle and implication in human diseases.



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 Ca^{2+} modulation of actin binding sites

Myosin binding sites blocked

Troponin- Ca^{2+} complex pulls tropomyosin away, exposing myosin binding sites

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Previous



Next



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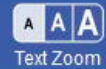
Notes



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Settings

A 55-year-old woman comes for evaluation of persistent morning stiffness. She was diagnosed with rheumatoid arthritis 4 months ago and was prescribed methotrexate. The patient currently takes the maximum tolerated dose, along with folic acid and as-needed naproxen. Vital signs are normal. On examination, swelling, tenderness, and pain on range of motion are found at the metacarpophalangeal and proximal interphalangeal joints and wrists bilaterally. Treatment with etanercept is considered. Which of the following tests should be performed before beginning treatment with this agent?

- ☐ A. Brain CT scan
- ☐ B. Echocardiogram
- ☐ C. Fecal occult blood test
- ☐ D. Pulmonary function tests
- ☐ E. Tuberculin skin test
- ☐ F. Visual examination

Submit

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End Block



A 55-year-old woman comes for evaluation of persistent morning stiffness. She was diagnosed with rheumatoid arthritis 4 months ago and was prescribed methotrexate. The patient currently takes the maximum tolerated dose, along with folic acid and as-needed naproxen. Vital signs are normal. On examination, swelling, tenderness, and pain on range of motion are found at the metacarpophalangeal and proximal interphalangeal joints and wrists bilaterally. Treatment with etanercept is considered. Which of the following tests should be performed before beginning treatment with this agent?

- ☐ A. Brain CT scan (0%)
- ☐ B. Echocardiogram (3%)
- ☐ C. Fecal occult blood test (2%)
- ☐ D. Pulmonary function tests (7%)
- ☒ E. Tuberculin skin test (83%)
- ☐ F. Visual examination (2%)





Mark



Previous



Next



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Lab Values



Notes



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Settings

Tumor necrosis factor-alpha (TNF- α) inhibitors are large-molecule anti-inflammatory agents ("biologics") commonly used to treat moderate to severe rheumatoid arthritis, particularly in patients who have failed methotrexate therapy. Etanercept is a fusion protein with domains derived from the Fc portion of IgG1 and TNF receptor 2. It functions as a **decoy receptor** for TNF- α . Other TNF- α inhibitors are anti-TNF monoclonal antibodies (eg, infliximab, adalimumab).

Inhibition of TNF- α leads to impaired cell-mediated immunity. In particular, TNF- α is necessary for effective sequestration of mycobacteria within granulomas. As a result, TNF- α inhibitors promote reactivation of latent tuberculosis and can increase the risk of disseminated disease. All patients being considered for TNF- α inhibitor therapy should have a baseline tuberculin skin test or interferon-gamma release assay to screen for latent tuberculosis. TNF- α inhibitors also increase susceptibility to other infectious agents, including fungi and atypical mycobacteria, and should not be used in any patient with an underlying infection.

(Choice A) CT is effective in diagnosing a variety of infections of the central nervous system, including disseminated tuberculosis. However, a baseline CT scan is not needed in rheumatoid arthritis in the absence of suspicious symptoms.



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Feedback



Suspend



End Block

absence of esophageal symptoms.

(Choice B) Baseline assessment of left ventricular function with echocardiogram or radionuclide ventriculography is recommended prior to treatment with anthracycline antineoplastic drugs (eg, doxorubicin).

(Choice C) Patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) are at increased risk for peptic ulcer. Fecal occult blood testing should be performed in patients taking NSAIDs whenever there is a clinical suspicion of gastrointestinal bleeding.

(Choice D) Pulmonary function tests may be important in patients taking medications known to cause pulmonary fibrosis, such as amiodarone. Methotrexate can cause both lung and liver toxicity, and a baseline chest x-ray and liver function tests are recommended.

(Choice F) Irreversible retinal damage can occur with long-term use of hydroxychloroquine. Patients starting hydroxychloroquine should have baseline and regular follow-up ophthalmologic examinations.

Educational objective:

Tumor necrosis factor-alpha (TNF- α) inhibitors impair cell-mediated immunity. All patients beginning treatment with TNF- α inhibitors should be evaluated for latent tuberculosis.

References



A 12-year-old girl comes to the office with constant swelling and pain of her elbows for the past week that have prevented her from participating in basketball practice. She also had knee pain during the preceding week that was attributed to a fall during practice. Her parents say that she is healthy and has had only minor illnesses that children typically experience during the winter. The patient's temperature is 38.9 C (102 F), blood pressure is 110/70 mm Hg, and pulse is 110/min. Her elbows are swollen and tender with limited range of movement. Her knees appear normal. A new holosystolic murmur is heard on cardiac auscultation. Antistreptolysin O titers are 400 Todd units/mL (normal: <300 Todd units/mL). The patient is admitted to the hospital. During her hospitalization, this patient is at greatest risk of dying from which of the following complications?

- ☐ A. Mitral stenosis
- ☐ B. Pancarditis
- ☐ C. Renal failure
- ☐ D. Septic arthritis
- ☐ E. Septic shock





week that was attributed to a fall during practice. Her parents say that she is healthy and has had only minor illnesses that children typically experience during the winter. The patient's temperature is 38.9 C (102 F), blood pressure is 110/70 mm Hg, and pulse is 110/min. Her elbows are swollen and tender with limited range of movement. Her knees appear normal. A new holosystolic murmur is heard on cardiac auscultation. Antistreptolysin O titers are 400 Todd units/mL (normal: <300 Todd units/mL). The patient is admitted to the hospital. During her hospitalization, this patient is at greatest risk of dying from which of the following complications?

- ☐ A. Mitral stenosis (6%)
- ☒ B. Pancarditis (49%)
- ☐ C. Renal failure (16%)
- ☐ D. Septic arthritis (3%)
- ☐ E. Septic shock (23%)

Correct

49%
Answered correctly01 min, 02 secs
Time Spent12/30/2020
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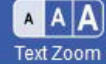
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Acute rheumatic fever

| | |
|--------------------------|--|
| Epidemiology | <ul style="list-style-type: none"> • Endemic in developing countries |
| Pathogenesis | <ul style="list-style-type: none"> • Occurs 2-4 weeks after acute group A streptococcal pharyngitis • Molecular mimicry: Anti-streptococcal antibodies attack cardiac & neuronal antigens |
| Clinical features | <ul style="list-style-type: none"> • Acute/subacute <ul style="list-style-type: none"> ◦ Migratory arthritis ◦ Pancarditis (mitral regurgitation) ◦ Sydenham chorea • Chronic <ul style="list-style-type: none"> ◦ Mitral stenosis |
| Prevention | <ul style="list-style-type: none"> • Prompt treatment of streptococcal pharyngitis with penicillin |

Acute rheumatic fever (ARF) is the most likely diagnosis in this patient with **migratory arthritis**, new-onset murmur, **fever**, and a **positive anti-streptolysin O titer**. ARF is a multisystem complication that develops



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Acute rheumatic fever (ARF) is the most likely diagnosis in this patient with **migratory arthritis**, new-onset murmur, **fever**, and a **positive anti-streptolysin O titer**. ARF is a multisystem complication that develops 2-4 weeks after untreated group A streptococcal pharyngitis. Most organs are often only mildly and transiently affected in ARF, with the exception of the heart. Acute morbidity is most likely due to pancarditis (inflammation of the endocardium, myocardium, and epicardium). Inflammation of the mitral valve can lead to **mitral regurgitation**, which is the likely cause of the new holosystolic murmur in this patient. Severe regurgitation and/or **myocarditis** can lead to cardiac dilation, **heart failure**, and death in a small percentage of patients.

(Choice A) Virtually all cases of mitral stenosis are caused by fibrosis of the valve leaflets in chronic rheumatic heart disease. The fibrosis occurs gradually over years or decades after the initial episode of ARF and would, therefore, not be an acute complication in this patient.

(Choice C) Acute poststreptococcal glomerulonephritis (PSGN) is caused by circulating immune complexes following a streptococcal pharyngeal infection with specific nephritogenic strains. Hematuria, edema, proteinuria, and hypertension are classic findings. This patient has no symptoms of PSGN, which rarely occurs simultaneously with ARF.

(Choice D) Patients with septic arthritis are often febrile and ill-appearing. *Staphylococcus aureus* is the



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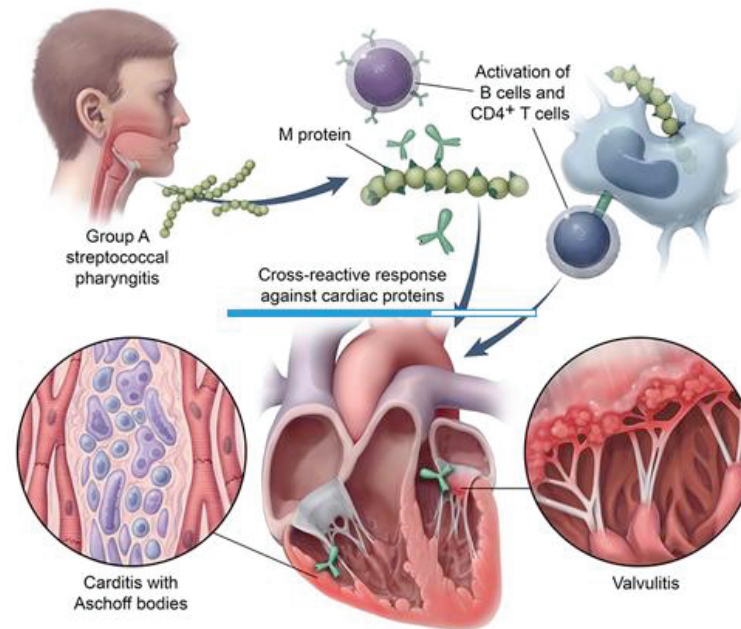
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Pathophysiology of acute rheumatic fever



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(Choice C) Acute poststreptococcal glomerulonephritis (PSGN) is caused by circulating immune

complexes following a streptococcal pharyngeal infection with specific nephritogenic strains. Hematuria, edema, proteinuria, and hypertension are classic findings. This patient has no symptoms of PSGN, which rarely occurs simultaneously with ARF.

(Choice D) Patients with septic arthritis are often febrile and ill-appearing. *Staphylococcus aureus* is the most common cause and usually infects only one joint.

(Choice E) Septic shock refers to end-organ damage due to poor perfusion from an overwhelming inflammatory response to infection. Although the pathogenesis of ARF involves an initial infection with group A *streptococcus*, the disease itself is autoimmune-related, not due to direct infection.

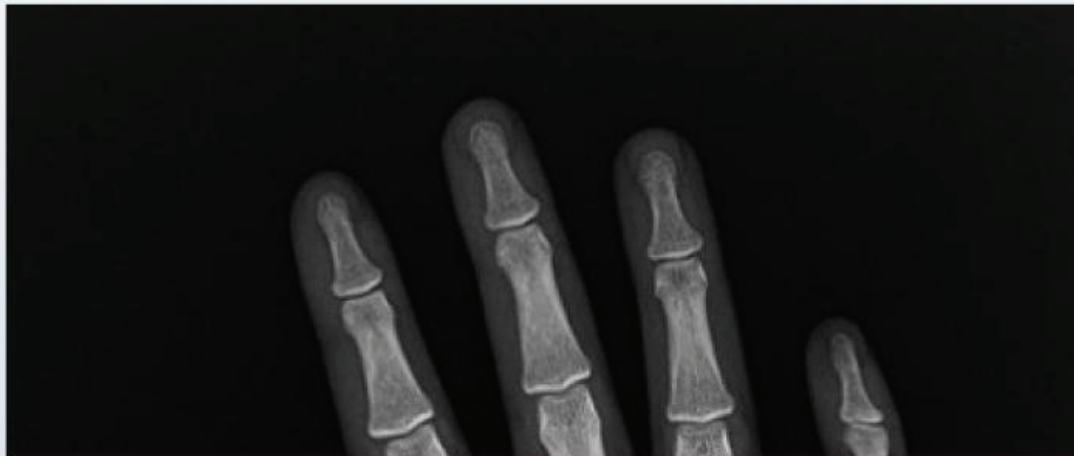
Educational objective:

The primary cause of morbidity in acute rheumatic fever is heart failure from severe pancarditis. Mitral stenosis develops years or decades after the original illness. Joint involvement is usually transient.

References

- Diagnostic criteria of acute rheumatic fever.
- Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Disease Society of America.

A 54-year-old woman comes to the emergency department due to a hand injury after a fall. The patient slipped in the bathroom and fell backwards onto her extended right hand. She was able to get up but has had right wrist pain and finger numbness since the fall. Medical history is notable for obesity, hypertension, and type 2 diabetes mellitus. On examination of her right hand, there is decreased sensation in the palmar aspect of her first three digits and a small bump is noted just below the palm. Lunate dislocation causing median nerve compression is suspected. Which of the following marked bones on a normal x-ray is most likely dislocated in this patient?





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Tutorial



Lab Values



Notes



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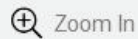


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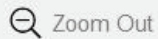


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☐ A.A☐ B.B☒ C.C☐ D.D☐ E.E**Submit**



- ☐ A.A (5%)
- ☐ B.B (6%)
- ☐ C.C (20%)
- ☒ D.D (64%)
- ☐ E.E (3%)

Correct

64%
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Time Spent02/06/2021
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Full Screen



Tutorial



Lab Values



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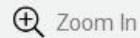


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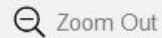


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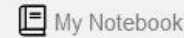
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This patient has **lunate dislocation** after a fall onto an outstretched hand (FOOSH). Although the force transmitted up the arm by a FOOSH can injure many different structures in the arm (eg, elbow, humerus, shoulder), wrist complications are the most common (eg, lunate or scaphoid dislocation/fracture, distal radius fracture).

The **lunate** is in the proximal row of **carpal bones** and can be identified on x-ray as the **more medial** (ulnar) of the 2 bones that **articulate with the radius**. Volar dislocation of the lunate can compress the median nerve within the carpal tunnel, resulting in wrist pain and numbness in the first (radial) 3½ digits.

(Choice A) The trapezium is the most lateral (radial) of the distal carpal bones and articulates with the first metacarpal.

(Choice B) The capitate is the largest carpal bone; it lies in the distal row at the center of the wrist and articulates with the third metacarpal.

(Choice C) The scaphoid is the most lateral (radial) of the proximal carpal bones and articulates with the radius. It is the carpal bone most frequently affected by a FOOSH; dislocation or fracture of the scaphoid can present with wrist pain and tenderness in the **anatomic snuffbox**. Scaphoid fractures have a high risk of avascular necrosis.





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Full Screen



Tutorial



Lab Values



Notes



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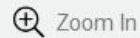
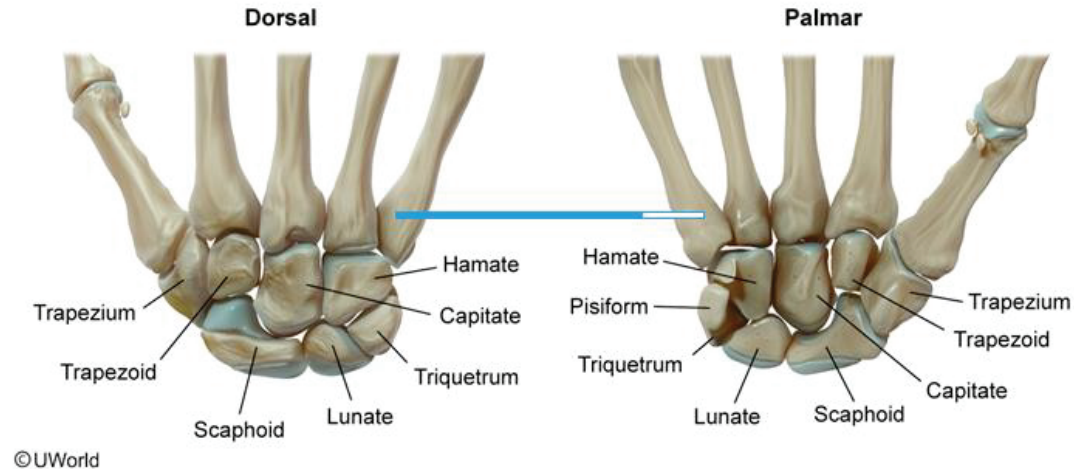
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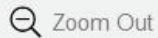
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Carpal bones



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Tutorial



Lab Values



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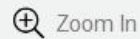
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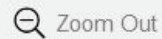
Anatomic snuffbox



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Feedback



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Tutorial

Lab Values

Notes

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(Choice B) The capitate is the largest carpal bone; it lies in the distal row at the center of the wrist and articulates with the third metacarpal.

(Choice C) The scaphoid is the most lateral (radial) of the proximal carpal bones and articulates with the radius. It is the carpal bone most frequently affected by a FOOSH; dislocation or fracture of the scaphoid can present with wrist pain and tenderness in the [anatomic snuffbox](#). Scaphoid fractures have a high risk of avascular necrosis.

(Choice E) The triquetrum is located in the proximal row on the medial (ulnar) side and is partially obscured on x-ray by the pisiform, which lies directly anterior to it.

Educational objective:

The lunate bone is the more medial (ulnar) of the 2 proximal carpal bones that articulate with the radius. A fall onto an outstretched hand can cause dislocation of the lunate bone with resulting compression of the median nerve (eg, wrist pain, numbness in the first 3½ digits).

Anatomy

Rheumatology/Orthopedics & Sports

Hand injury

Subject

System

Topic

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A 55-year-old man comes to the office for evaluation of chronic muscle weakness. Over the past several months, he has had increasing difficulty walking up stairs and lately has had trouble removing objects out of the overhead cabinets in his kitchen. Temperature is 36.7 C (98 F), blood pressure is 125/80 mm Hg, and pulse is 78/min. On examination, the patient has symmetric proximal muscle weakness and mild muscle tenderness. There is no rash. Muscle biopsy reveals an endomysial mononuclear infiltrate and patchy muscle fiber necrosis. An autoantibody directed against which of the following antigens is most likely to be seen in this patient?

- ☐ A. Acetylcholine receptor
- ☐ B. Cardiolipin
- ☐ C. Desmoglein
- ☐ D. Mitochondria
- ☐ E. Presynaptic calcium channel
- ☐ F. tRNA synthetase
- ☐ G. Smooth muscle

months, he has had increasing difficulty walking up stairs and lately has had trouble removing objects out of the overhead cabinets in his kitchen. Temperature is 36.7 C (98 F), blood pressure is 125/80 mm Hg, and pulse is 78/min. On examination, the patient has symmetric proximal muscle weakness and mild muscle tenderness. There is no rash. Muscle biopsy reveals an endomysial mononuclear infiltrate and patchy muscle fiber necrosis. An autoantibody directed against which of the following antigens is most likely to be seen in this patient?

- ☐ A. Acetylcholine receptor (8%)
- ☐ B. Cardiolipin (4%)
- ☐ C. Desmoglein (16%)
- ☒ D. Mitochondria (13%)
- ☐ E. Presynaptic calcium channel (10%)
- ☒ F. tRNA synthetase (38%)
- ☐ G. Smooth muscle (7%)

Polymyositis

Clinical presentation

- Symmetrical proximal **muscle weakness**
- Increasing difficulty climbing stairs, getting up from a chair, carrying heavy objects

Pathologic features

- **Elevated muscle enzymes** (CK, aldolase)
- Autoantibodies (ANA, anti-Jo-1)
- **Biopsy**: Endomysial mononuclear infiltrate, patchy necrosis

Associated complications

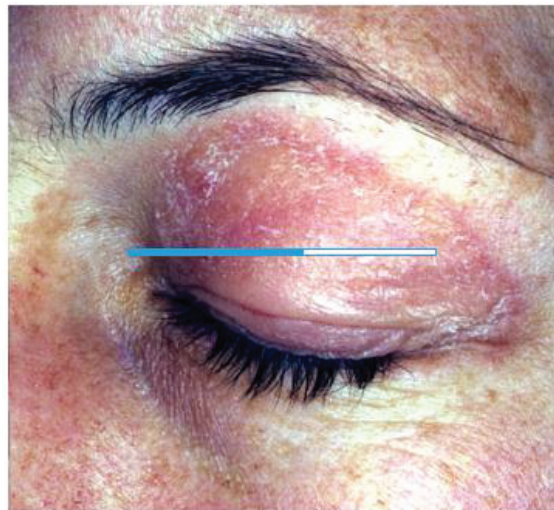
- Interstitial lung disease
- Myocarditis

ANA = antinuclear antibodies; **CK** = creatine kinase.

Polymyositis is an inflammatory myopathy that typically presents in middle age with an insidious onset of symmetric **proximal muscle weakness** affecting the upper and lower extremities without significant pain. Dermatomyositis is a similar disorder associated with characteristic **skin findings**. Both polymyositis and dermatomyositis may occur independently or as a paraneoplastic manifestation of an underlying

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Dermatomyositis Gottron's papules



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Dermatomyositis [Gotttron's papules](#)

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Dermatomyositis is a similar disorder associated with characteristic **skin findings**. Both polymyositis and dermatomyositis may occur independently or as a paraneoplastic manifestation of an underlying malignancy (especially **adenocarcinoma**).

Muscle enzyme (eg, creatine kinase, aldolase) levels in inflammatory myopathies are invariably elevated. Autoantibodies, especially antinuclear antibodies, are also present in most cases; anti-histidyl-**tRNA synthetase (anti-Jo-1)** antibodies are less sensitive but more specific for dermatomyositis and polymyositis. A biopsy can differentiate polymyositis from dermatomyositis, which typically shows an **endomysial inflammation** without prominent vascular involvement in a scattered or patchy distribution (in contrast, dermatomyositis causes *perifascicular inflammation* in a segmental pattern without vasculopathy).

(Choices A and E) Acetylcholine receptor-binding antibodies occur in myasthenia gravis, which is characterized by episodic weakness that initially affects the ocular/bulbar musculature and worsens with repetition. Antibodies to voltage-gated calcium channels cause Lambert-Eaton myasthenic syndrome (proximal muscle weakness that improves with isometric contraction), which is often associated with small cell lung cancer. Muscle biopsy in these conditions is normal.

(Choice B) Anticardiolipin antibodies are typically seen in antiphospholipid antibody syndrome, which is characterized by recurrent vascular thrombosis and/or pregnancy loss. This syndrome is associated with

cell lung cancer. Muscle biopsy in these conditions is normal.

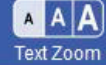
(Choice B) Anticardiolipin antibodies are typically seen in antiphospholipid antibody syndrome, which is characterized by recurrent vascular thrombosis and/or pregnancy loss. This syndrome is associated with systemic lupus erythematosus, although it may occur independently.

(Choice C) Autoantibodies to desmoglein 1 and 3 are seen in patients with pemphigus vulgaris, which is characterized by skin blistering and desquamation.

(Choices D and G) Antimitochondrial antibodies are seen in patients with primary biliary cholangitis, which presents with cholestatic symptoms (eg, pruritus, jaundice, steatorrhea) and abnormal hepatic enzyme levels. Anti-smooth muscle antibodies are seen in autoimmune hepatitis, which most commonly presents as chronic progressive hepatitis in middle-aged women.

Educational objective:

Polymyositis and dermatomyositis are characterized by symmetric proximal muscle weakness and are associated with antinuclear and anti-tRNA synthetase (anti-Jo-1) autoantibodies. Biopsy in polymyositis shows patchy endomysial inflammatory infiltrate (ie, direct invasion of individual muscle fibers), whereas dermatomyositis causes perifascicular inflammation (ie, localized around blood vessels and the septa between muscle fascicles).



A 24-year-old man comes to the office due to severe pain in the posterior aspect of the right foot that interferes with walking. For the last several months, the patient has also experienced a dull backache and morning stiffness that is relieved by over-the-counter ibuprofen. Family history is insignificant, and he does not use tobacco, alcohol, or illicit drugs. Which of the following is the most probable location of the pathologic process responsible for this patient's foot pain?

- ☐ A. Articular cartilage
- ☐ B. Cortical bone
- ☐ C. Periarticular bursae
- ☐ D. Synovial membrane
- ☐ E. Tendon insertion site


Submit



A 24-year-old man comes to the office due to severe pain in the posterior aspect of the right foot that interferes with walking. For the last several months, the patient has also experienced a dull backache and morning stiffness that is relieved by over-the-counter ibuprofen. Family history is insignificant, and he does not use tobacco, alcohol, or illicit drugs. Which of the following is the most probable location of the pathologic process responsible for this patient's foot pain?

- ☐ A. Articular cartilage (12%)
- ☐ B. Cortical bone (7%)
- ☐ C. Periarticular bursae (3%)
- ☐ D. Synovial membrane (12%)
- ☒ E. Tendon insertion site (63%)

Correct

 63%
Answered correctly 01 min, 03 secs
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| Enthesitis | |
|---------------------------------|---|
| Location of inflammation | <ul style="list-style-type: none">• Sites of mechanical stress• Insertion of tendons, ligaments, joint capsules |
| Common presentations | <ul style="list-style-type: none">• Achilles tendinitis (posterior heel pain)• Plantar fasciitis (plantar heel pain)• Dactylitis ("sausage digits") |
| Disease associations | <ul style="list-style-type: none">• Ankylosing spondylitis• Psoriasis/psoriatic arthritis• Reactive arthritis |

This patient has inflammatory back pain (ie, onset at age <40, chronic/insidious pain and stiffness that are better with activity and worse with rest), which is likely due to **ankylosing spondylitis (AS)**.

In AS, the inflammatory process is thought to originate in the gut due to an altered intestinal biome and defects in the mucosal barrier; the resulting inflammatory response leads to upregulation of cytokines (primarily tumor necrosis factor-alpha and IL-17), with activation of innate immunity and migration of



(primarily tumor necrosis factor-alpha and IL-17), with activation of innate immunity and migration of immune cells to the skeleton. The resulting **skeletal manifestations** are most prominent in areas of **mechanical stress**, primarily at the **insertions of tendons**, ligaments, and joint capsules (collectively, entheses) on bone.

Enthesitis is a relatively specific finding in AS and other forms of spondyloarthritis and is characterized by local pain, tenderness, and possible swelling. Common clinical syndromes include Achilles tendinitis, plantar fasciitis, and dactylitis ("sausage digits"). **Achilles tendinitis** affects the site of insertion of the Achilles tendon on the calcaneus and typically presents with severe pain at the **posterior aspect of the heel**.

(Choices A and D) Peripheral arthritis is common in AS. In these cases, the inflammatory process largely affects the articular cartilage and subchondral bone; synovial involvement is typically minor. However, the pain is typically felt within the ankle (eg, tibiotalar and subtalar arthritis) rather than at the posterior aspect of the foot.

(Choice B) Injury to the cortical bone of the calcaneus can occur acutely due to a high-velocity fall or crush injury or chronically due to a stress fracture in athletes who run on hard surfaces. This patient's inflammatory back pain makes enthesitis a more likely cause of his heel pain.



of the foot.

(Choice B) Injury to the cortical bone of the calcaneus can occur acutely due to a high-velocity fall or crush injury or chronically due to a stress fracture in athletes who run on hard surfaces. This patient's inflammatory back pain makes enthesitis a more likely cause of his heel pain.

(Choice C) Retrocalcaneal bursitis causes pain and swelling at the posterior heel near the insertion of the Achilles tendon. It is usually caused by overuse and often occurs in association with Achilles tendinopathy. However, it is significantly less common than enthesitis as a cause of posterior heel pain in AS.

Educational objective:

Enthesitis (inflammation at the bony insertions of tendons, ligaments, and joint capsules) is a prominent manifestation of spondyloarthritis (eg, ankylosing spondylitis). Common clinical syndromes include Achilles tendinitis, plantar fasciitis, and dactylitis. Achilles tendinitis affects the site of insertion of the Achilles tendon on the calcaneus and presents with severe pain at the posterior aspect of the foot.

References

- [Review: enthesitis: new insights into pathogenesis, diagnostic modalities, and treatment.](#)

Pathophysiology Rheumatology/Orthopedics & Sports Ankylosing spondylitis

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A 55-year-old man is admitted to the hospital due to abdominal discomfort and black stools. Medical history includes asthma and hypertriglyceridemia, for which the patient takes the appropriate medications. He has smoked a pack of cigarettes daily for 30 years and used intravenous drugs in the past. The patient is treated empirically with a proton pump inhibitor; upper gastrointestinal endoscopy does not reveal a source for the pain or bleeding. Symptoms resolve without further intervention, and he is discharged. Several weeks later, the patient returns to the emergency department with fever, weight loss, and muscle pain. After initial evaluation, muscle biopsy demonstrates transmural inflammation of medium-sized arteries with areas of amorphous, eosin-staining arterial wall necrosis. Areas of disruption of the internal elastic lamina are also present. Which of the following is the most likely predisposing factor for this patient's current condition?

- ☐ A. Antibiotic use
- ☐ B. Asthma
- ☐ C. Hypertriglyceridemia
- ☐ D. Smoking
- ☐ E. Viral hepatitis





history includes asthma and hypertriglyceridemia, for which the patient takes the appropriate medications.

He has smoked a pack of cigarettes daily for 30 years and used intravenous drugs in the past. The patient is treated empirically with a proton pump inhibitor; upper gastrointestinal endoscopy does not reveal a source for the pain or bleeding. Symptoms resolve without further intervention, and he is discharged. Several weeks later, the patient returns to the emergency department with fever, weight loss, and muscle pain. After initial evaluation, muscle biopsy demonstrates transmural inflammation of medium-sized arteries with areas of amorphous, eosin-staining arterial wall necrosis. Areas of disruption of the internal elastic lamina are also present. Which of the following is the most likely predisposing factor for this patient's current condition?

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- ☐ E. Viral hepatitis



is treated empirically with a proton pump inhibitor; upper gastrointestinal endoscopy does not reveal a source for the pain or bleeding. Symptoms resolve without further intervention, and he is discharged. Several weeks later, the patient returns to the emergency department with fever, weight loss, and muscle pain. After initial evaluation, muscle biopsy demonstrates **transmural inflammation** of medium-sized arteries with areas of amorphous, eosin-staining arterial wall necrosis. Areas of disruption of the internal elastic lamina are also present. Which of the following is the most likely predisposing factor for this patient's current condition?

- ☐ A. Antibiotic use (3%)
- ☐ B. Asthma (5%)
- ☐ C. Hypertriglyceridemia (8%)
- ☒ D. Smoking (40%)
- ☐ E. Viral hepatitis (41%)

Incorrect

Correct answer

41%

Answered correctly



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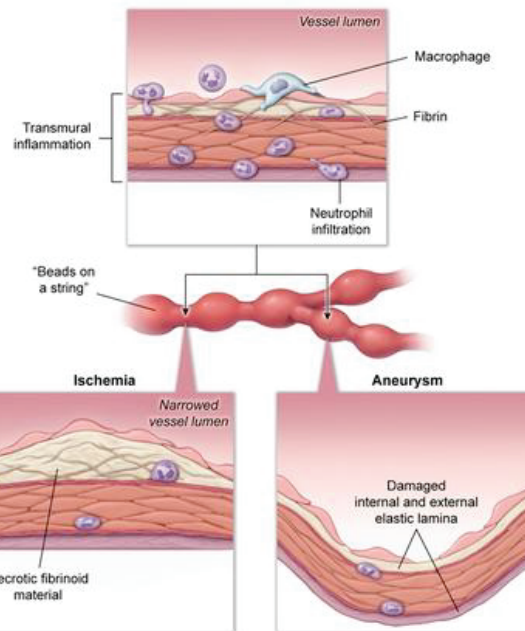
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Polyarteritis nodosa



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This patient's biopsy is consistent with **polyarteritis nodosa (PAN)**, a systemic vasculitis of **medium-sized muscular arteries**. Patients with PAN typically present with weeks or months of **constitutional symptoms** (eg, malaise, weight loss, myalgia, fever) and signs of tissue **ischemia** in the kidneys, skin, gastrointestinal tract, and/or neurologic system. Bleeding complications may occur due to the formation of **microaneurysms** from arterial wall weakening. Biopsy of affected areas generally reveals **segmental, transmural inflammation** with **fibrinoid necrosis** (amorphous, eosinophilic material in vessel wall) and disruption of the internal and external **elastic laminae**.

In contrast to many other forms of vasculitis, PAN is not associated with antineutrophil cytoplasmic antibodies or significantly elevated antinuclear antibody titers. However, inflammatory markers (eg, C-reactive protein, erythrocyte sedimentation rate) are generally high. Although many cases of PAN have no clear inciting factor, up to a third of patients have underlying **viral hepatitis B or C**. In these individuals, PAN is likely triggered by the deposition of **immune complexes** (viral antigen bound by host antibody) in the arterial wall.

(Choice A) Cutaneous small-vessel (leukocytoclastic) vasculitis is frequently triggered by antibiotic use. This condition is also mediated by immune complexes and often causes fibrinoid necrosis of the vessel wall. However, most cases are marked by palpable purpura and disease is limited to small (not medium-



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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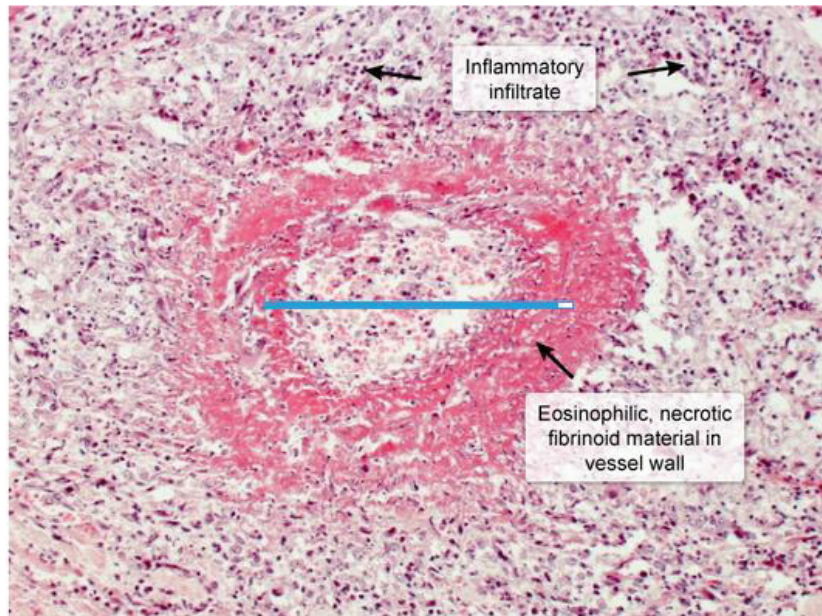
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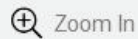
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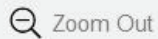
Polyarteritis nodosa



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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) Eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome) causes asthma and allergic rhinosinusitis. Biopsy generally shows **eosinophilic infiltration** in the vessel wall with granulomas. Small arteries and veins are primarily affected, and antineutrophil cytoplasmic antibodies are often positive.

(Choice C) Severe hypertriglyceridemia can cause abdominal pain due to acute pancreatitis, but transmural vascular inflammation with fibrinoid necrosis would be atypical.

(Choice D) Thromboangiitis obliterans (Buerger disease) occurs primarily in young smokers and is marked by limb claudication or digital ulcers. Biopsy typically shows highly cellular, inflammatory thrombi in small- to medium-sized vessels of the extremities; there is limited involvement of the vessel wall (eg, intact internal elastic lamina, no fibrinoid necrosis).

Educational objective:

Polyarteritis nodosa (PAN) is a systemic vasculitis characterized by constitutional manifestations and ischemic symptoms in the kidneys, skin, gastrointestinal tract, and neurologic system. Biopsy will show segmental, transmural arterial inflammation with fibrinoid necrosis and damage to the internal and external elastic lamina. PAN is often associated with underlying viral hepatitis B and C.

References





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

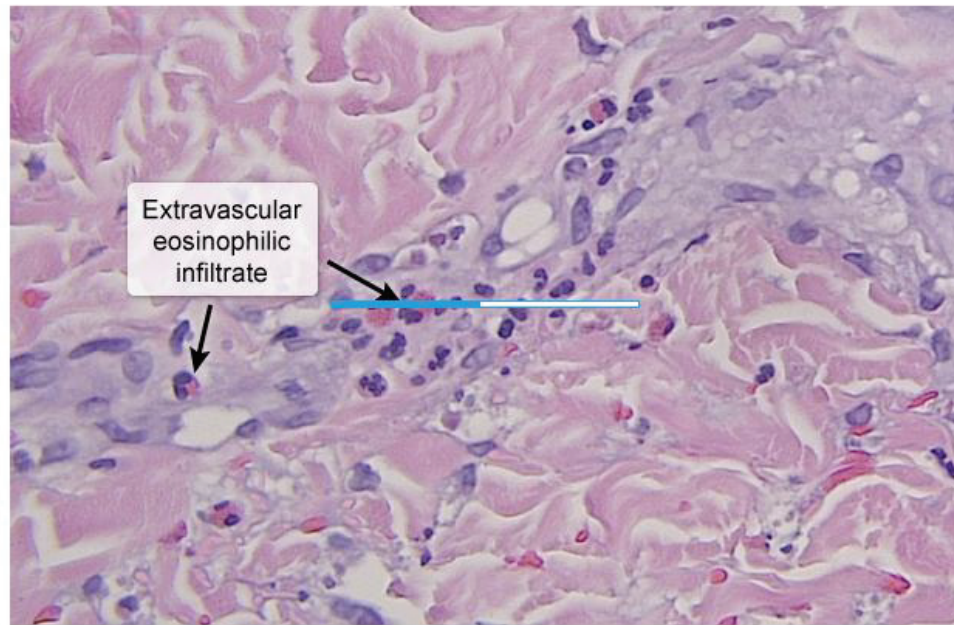
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(Choice B) Eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome) causes

Exhibit Display

Eosinophilic granulomatosis with polyangiitis



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End Block

A 17-year-old girl is brought to the office for evaluation of a right wrist mass. She noticed swelling on the top of her wrist approximately 3 months ago but said that it did not bother her until she was teased about it in school. She has no other concerns. Examination shows a nontender, rounded mass on the dorsal wrist that transilluminates with a penlight. An image of the mass is shown below:

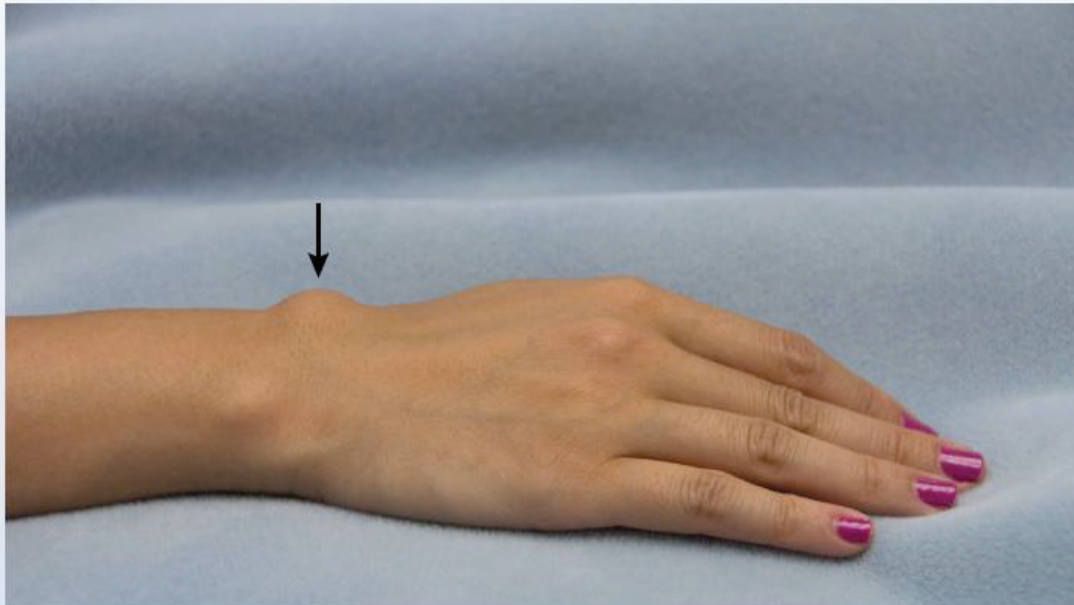
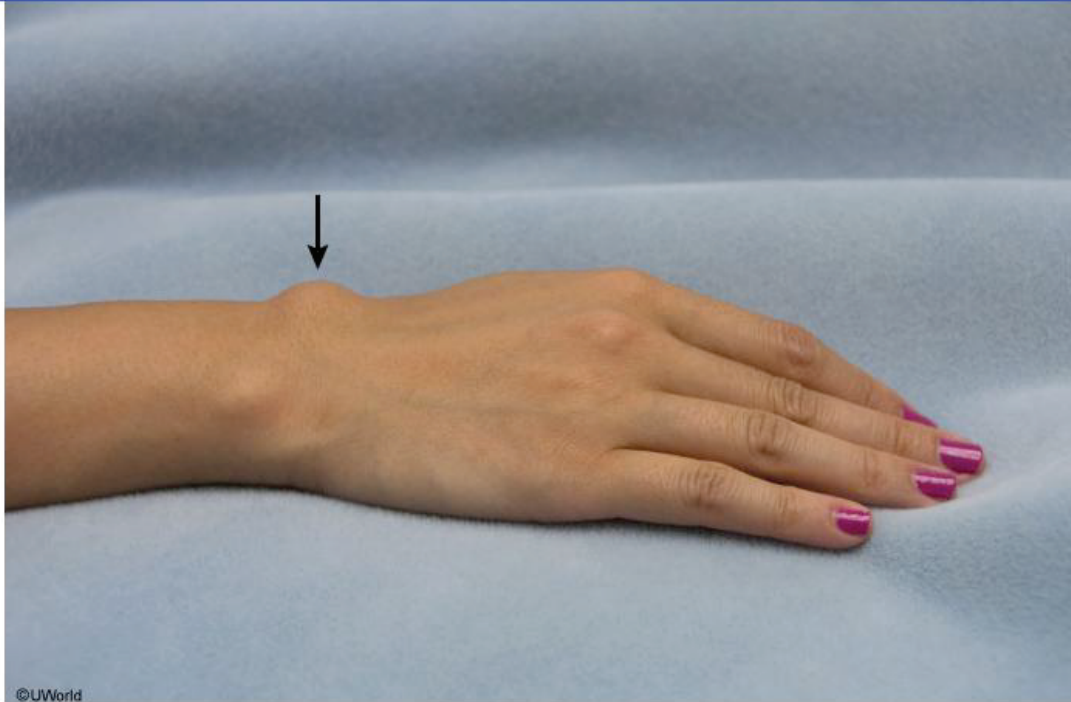


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Which of the following is the most likely underlying etiology?

- ☐ A. Benign proliferation of fat cells
- ☐ B. Degeneration of periarticular tissue
- ☐ C. Immune-mediated joint destruction
- ☐ D. Malignant transformation of synovial tissue
- ☐ E. Uric acid crystal deposition

Submit



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Which of the following is the most likely underlying etiology?

- ☐ A. Benign proliferation of fat cells (57%)
- ☒ B. Degeneration of periarticular tissue (30%)
- ☐ C. Immune-mediated joint destruction (2%)
- ☐ D. Malignant transformation of synovial tissue (9%)
- ☐ E. Uric acid crystal deposition (1%)

Correct

30%



23 secs



03/06/2021

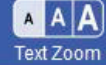


Ganglion cyst

| | |
|------------------------|--|
| Pathophysiology | <ul style="list-style-type: none">• Mucoïd degeneration of periarticular tissue• Mucinous fluid collects via a 1-way valve mechanism |
| Presentation | <ul style="list-style-type: none">• Usually painless but can cause mild aching or compressive symptoms• Smooth, rubbery, round structure that overlies a joint or tendon & transilluminates |
| Management | <ul style="list-style-type: none">• Usually resolves spontaneously |

This patient has a **ganglion cyst**, a benign, fluid-filled mass that overlies a joint or tendon. Ganglion cysts occur most commonly on the dorsal wrist; other common sites include the volar wrist, digits, and feet. They are thought to be due to **mucoïd degeneration of periarticular tissue**, leading to outpouching of the connective tissue. Mucinous fluid collects via a 1-way valve mechanism, possibly due to repetitive joint movements, resulting in slow growth of the cyst.

Ganglion cysts are usually **painless**, and most patients seek medical attention because of cosmetic concerns or fear of malignancy. However, some patients may experience mild aching, and significant compression can occasionally result in numbness or weakness. Physical examination reveals a smooth



Ganglion cysts are usually **painless**, and most patients seek medical attention because of cosmetic concerns or fear of malignancy. However, some patients may experience mild aching, and significant compression can occasionally result in paresthesia or weakness. Physical examination reveals a **smooth**, rubbery, **round structure** that overlies a joint or tendon and **transilluminates** with a penlight. Most ganglion cysts **resolve spontaneously** without intervention.

(Choice A) **Lipomas** are benign neoplasms caused by the proliferation of fat cells. Although they can occur on the wrist, they most commonly present on the trunk or proximal arms. Lipomas do not transilluminate.

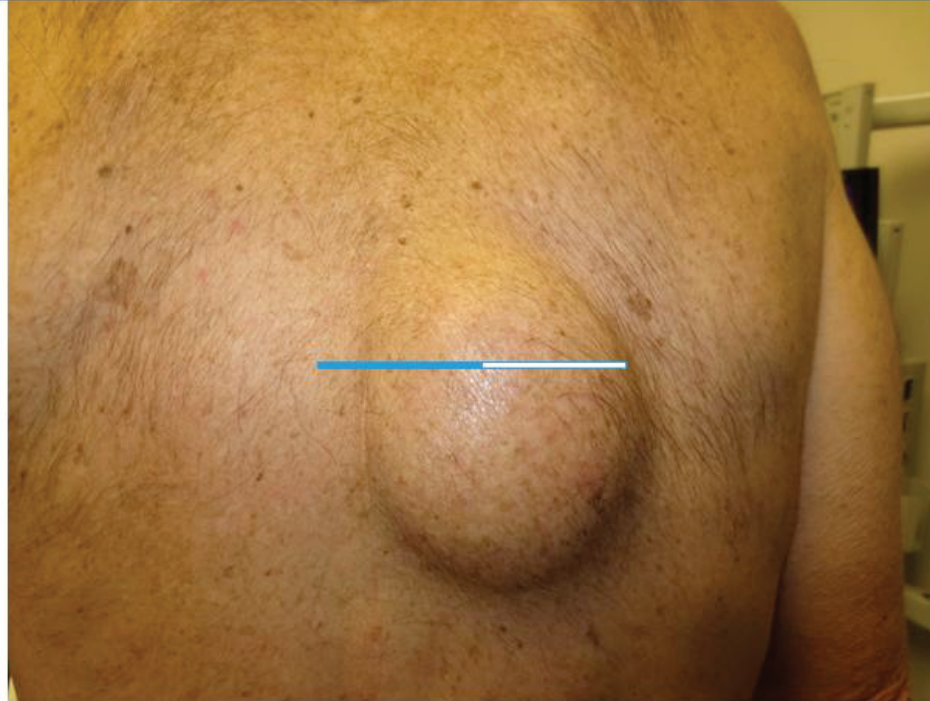
(Choice C) Rheumatoid arthritis (RA) is characterized by immune-mediated joint destruction. It can be associated with rheumatoid nodules, which present as **nontender subcutaneous nodules** over pressure points (eg, olecranon process). However, rheumatoid nodules do not transilluminate, and patients with RA typically have symmetric joint swelling and pain in the small joints of the hands and wrists, as well as characteristic joint deformities (eg, **ulnar deviation**).

(Choice D) Synovial sarcoma occurs from the malignant transformation of synovial tissue and can cause isolated swelling along the tendons. However, it does not transilluminate.

(Choice E) **Tophi** occur from chronic uric acid deposition and present with firm, nontender subcutaneous



Exhibit Display



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(Choice E) tophi occur from chronic uric acid deposition and present with firm, nontender subcutaneous

Exhibit Display



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(Choice E) tophi occur from chronic uric acid deposition and present with firm, nontender subcutaneous

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(Choice E) tophi occur from chronic uric acid deposition and present with firm, nontender subcutaneous

associated with rheumatoid nodules, which present as **nontender subcutaneous nodules** over pressure points (eg, olecranon process). However, rheumatoid nodules do not transilluminate, and patients with RA typically have symmetric joint swelling and pain in the small joints of the hands and wrists, as well as characteristic joint deformities (eg, **ulnar deviation**).

(Choice D) Synovial sarcoma occurs from the malignant transformation of synovial tissue and can cause isolated swelling along the tendons. However, it does not transilluminate.

(Choice E) **Tophi** occur from chronic uric acid deposition and present with firm, nontender subcutaneous nodules that are often yellow tinged; they do not transilluminate. In addition, patients usually have a history of recurrent gout flares (ie, exquisitely painful, swollen, erythematous joint).

Educational objective:

Ganglion cysts are benign, fluid-filled masses that occur due to mucoid degeneration of periarticular tissue. They present as painless, smooth, rubbery, round structures that overlie joints (eg, wrist) or tendons and transilluminate with a penlight. Most resolve spontaneously without intervention.

Pathophysiology
Subject

Rheumatology/Orthopedics & Sports
System

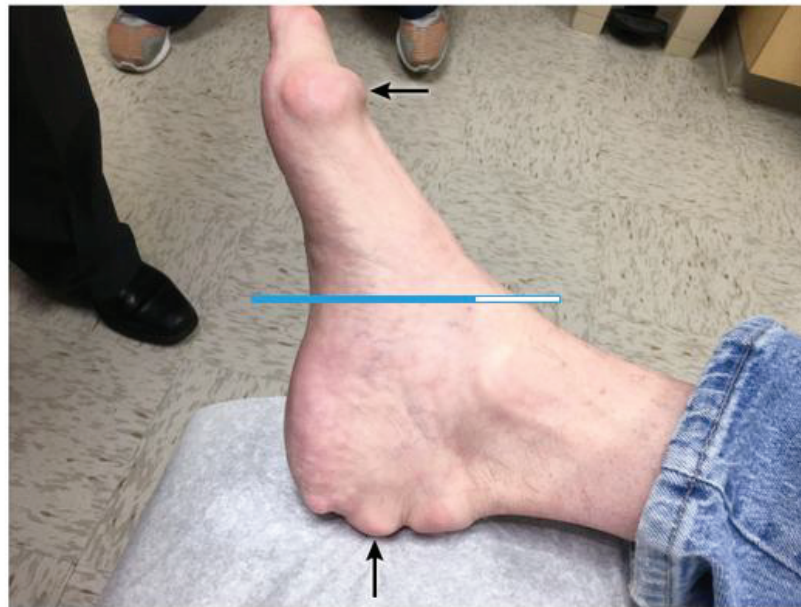
Ganglion cyst
Topic

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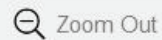
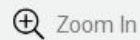
associated with rheumatoid nodules, which present as nontender subcutaneous nodules over pressure

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Gouty tophi



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A 56-year-old man comes to the urgent care center with severe knee pain. He was feeling well until he awoke this morning with acute pain, redness, and swelling in the knee. The patient does not smoke but did drink heavily at a wedding reception the night before. Past medical history is notable for recent peptic ulcer disease. He is treated with oral colchicine and experiences significant relief of symptoms within 12 hours. The drug used in this patient most likely affects which of the steps shown in the diagram below?

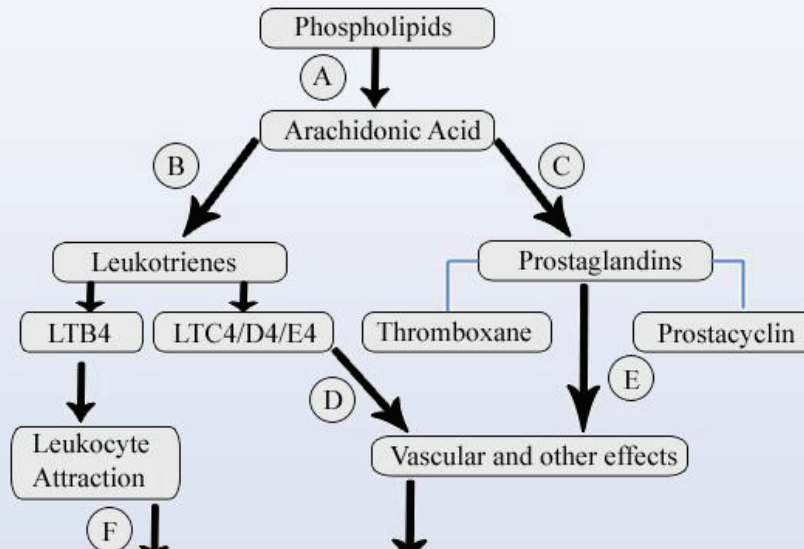
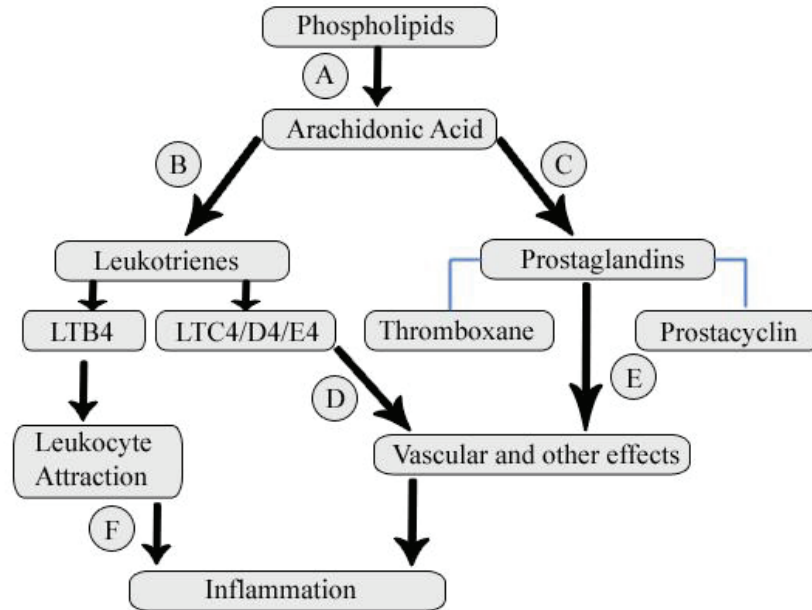
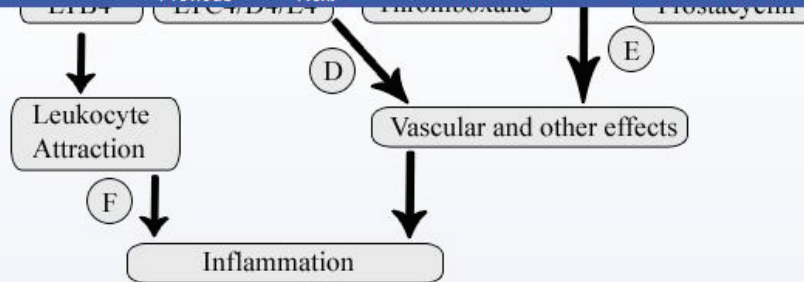


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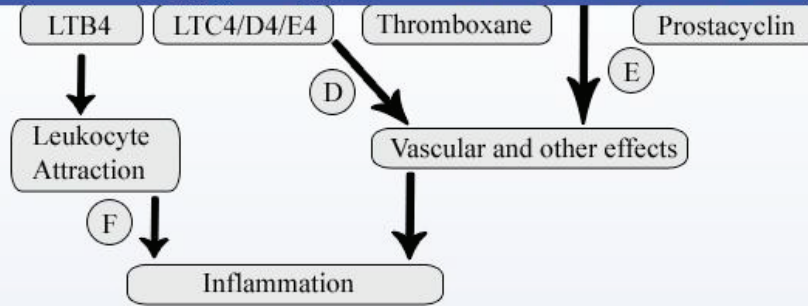


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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E
- ☐ F.F

Submit



- ☐ A.A (6%)
- ☐ B.B (5%)
- ☐ C.C (9%)
- ☒ D.D (2%)
- ☐ E.E (4%)
- ☒ F.F (70%)

Incorrect

70%

55 secs

01/15/2021

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Feedback

Suspend

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Mark



Previous



Next



Full Screen



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Lab Values



Notes



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This patient with acute atraumatic monoarticular arthritis involving the knee has typical symptoms of **gout**. The usual first-line treatment of acute gouty arthritis is nonsteroidal anti-inflammatory drugs (NSAIDs) (eg, indomethacin), but these are relatively contraindicated in patients with a history of peptic ulcer. **Colchicine** can also be used to treat acute gouty arthritis and results in resolution of symptoms in most patients.

Colchicine works primarily by inhibiting **microtubular polymerization**. It binds to the tubulin protein that helps form microtubules, preventing their aggregation. This in turn disrupts cytoskeletal-dependent functions such as **chemotaxis, phagocytosis, and degranulation**. Colchicine also reduces the formation of leukotriene B₄. It does not have any effect on the metabolism or urinary excretion of uric acid. Important adverse effects of colchicine are nausea, abdominal pain, and diarrhea. Colchicine should not be used in elderly patients or those with severe renal dysfunction.

(Choices A and E) Glucocorticoids inhibit the enzyme phospholipase A₂, which converts membrane phospholipids to arachidonic acid. This in turn decreases the formation of inflammatory prostaglandins and leukotrienes. Glucocorticoids can be given systemically or by intra-articular injection for treatment of gout in patients who cannot take NSAIDs or colchicine.

(Choices B and D) The **leukotriene pathways** can be blocked by inhibiting the 5-lipoxygenase pathway or



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in patients who cannot take NSAIDs or colchicine.

(Choices B and D) The **leukotriene pathways** can be blocked by inhibiting the 5-lipoxygenase pathway or by blocking the leukotriene receptors. Zileuton is a specific inhibitor of the enzyme 5-lipoxygenase and inhibits leukotriene formation (LTB_4 , LTC_4 , LTD_4 , and LTE_4). Montelukast inhibits LTD_4 receptors. Leukotriene modifiers are used in the treatment of asthma and allergic rhinitis but have no role in the treatment of gout.

(Choice C) Cyclooxygenase (COX) catalyzes the conversion of arachidonic acid to prostanoids. It exists in 2 isoforms, COX-1 and COX-2. COX-2 is an inducible enzyme that is upregulated in inflammatory cells to increase synthesis of pro-inflammatory arachidonic acid metabolites. Standard NSAIDs (eg, indomethacin, ibuprofen) inhibit both COX-1 and COX-2, while selective COX-2 inhibitors (eg, celecoxib) inhibit only COX-2.

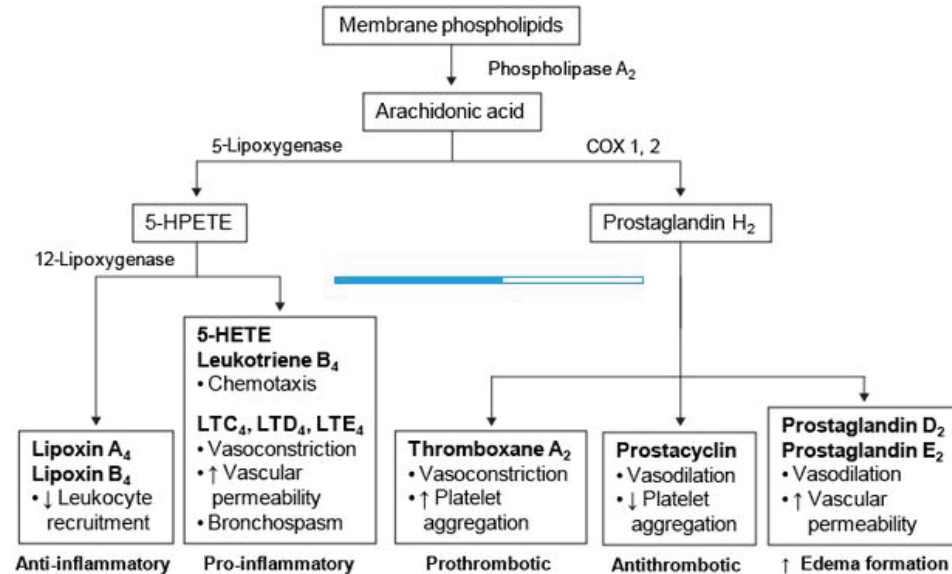
Educational objective:

Colchicine is used for treatment of acute gouty arthritis in patients who cannot take nonsteroidal anti-inflammatory drugs. It inhibits leukocyte migration and phagocytosis by blocking tubulin polymerization. Significant side effects of colchicine include nausea and diarrhea.

References

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Arachidonic acid metabolic pathways



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References

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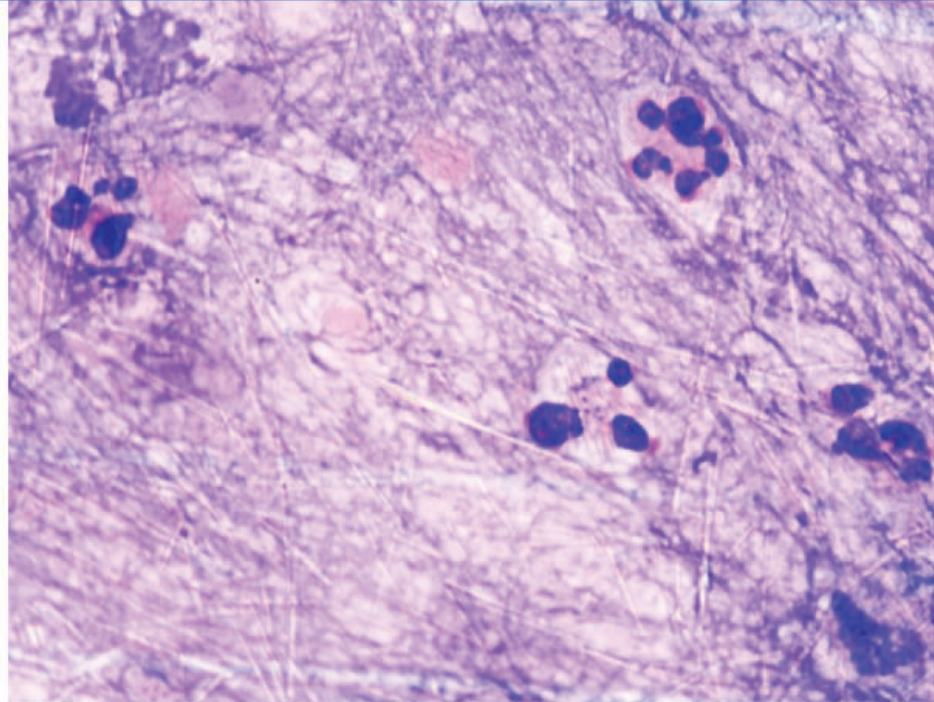
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A 36-year-old man comes to the emergency department due to severe, acute knee pain that awoke him from sleep. He has a history of end-stage renal disease for which he underwent a renal transplant 8 weeks ago. The patient takes an immunosuppressive regimen that includes cyclosporine and low-dose prednisone. He visited his nephrologist last week and serum creatinine levels were normal with no proteinuria. Temperature is 37.5 C (99.5 F), blood pressure is 136/78 mm Hg, and pulse is 88/min. Examination shows redness, warmth, and a small effusion in the left knee. Passive range of motion at the knee causes severe pain. Microscopic examination of joint fluid from the knee shows numerous neutrophils as well as both intra- and extracellular crystals as shown in the [exhibit](#). Which of the following mechanisms is most likely responsible for this patient's acute symptoms?

- ☐ A. Decreased urinary excretion of uric acid
- ☐ B. Increased production of uric acid
- ☐ C. Rapid drop in blood uric acid levels
- ☐ D. Release of nucleic acids from apoptotic cells
- ☐ E. Volume depletion and decreased renal perfusion

Exhibit Display



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ago. The patient takes an immunosuppressive regimen that includes cyclosporine and low-dose prednisone. He visited his nephrologist last week and serum creatinine levels were normal with no proteinuria. Temperature is 37.5 C (99.5 F), blood pressure is 136/78 mm Hg, and pulse is 88/min. Examination shows redness, warmth, and a small effusion in the left knee. Passive range of motion at the knee causes severe pain. Microscopic examination of joint fluid from the knee shows numerous neutrophils as well as both intra- and extracellular crystals as shown in the exhibit. Which of the following mechanisms is most likely responsible for this patient's acute symptoms?



- ☒ A. Decreased urinary excretion of uric acid (48%)
- ☐ B. Increased production of uric acid (23%)
- ☐ C. Rapid drop in blood uric acid levels (3%)
- ☐ D. Release of nucleic acids from apoptotic cells (21%)
- ☐ E. Volume depletion and decreased renal perfusion (3%)

Correct



48%

Answered correctly



01 min, 49 secs

Time spent



11/11/2020

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Medications associated with gout

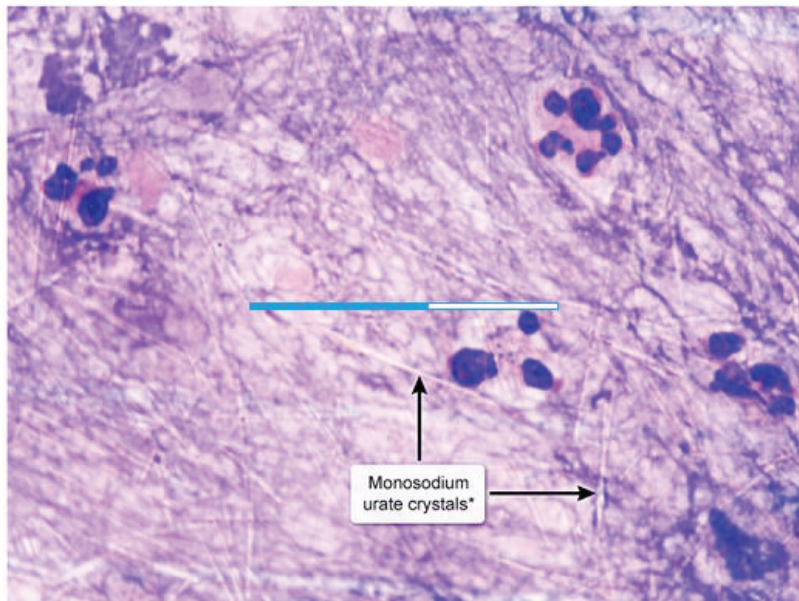
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| Reduced uric acid excretion | <ul style="list-style-type: none">• Diuretics (eg, hydrochlorothiazide, furosemide)• Salicylates (eg, low-dose aspirin)• ACE inhibitors (eg, lisinopril)• Cyclosporine |
| Increased uric acid production | <ul style="list-style-type: none">• Cytotoxic chemotherapy agents (tumor lysis syndrome) |
| Rapid decline in uric acid levels | <ul style="list-style-type: none">• Xanthine oxidase inhibitors (eg, allopurinol)• Uricosuric drugs (eg, probenecid) |

This patient has acute monoarticular arthritis of the knee with synovial fluid evidence of inflammation and **needle-shaped** (monosodium urate) crystals, indicating a diagnosis of **gout**. Gout develops in patients with **hyperuricemia** and is associated with several risk factors including excessive alcohol intake, meat/seafood consumption, chronic kidney disease, and certain medications.

Cyclosporine is a common cause of gout exacerbations in patients who have undergone solid organ transplantation, particularly renal transplantation. This medication **impairs renal excretion of uric acid**, resulting in hyperuricemia. Although high doses of systemic glucocorticoids (eg, prednisone) can be used

Exhibit Display

Gout



*Needle-shaped crystals

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Cyclosporine is a common cause of gout exacerbations in patients who have undergone solid organ transplantation, particularly renal transplantation. This medication **impairs renal excretion of uric acid**, resulting in hyperuricemia. Although high doses of systemic glucocorticoids (eg, prednisone) can be used to treat acute gout, the low doses used for immunosuppression in patients who have undergone transplantation are usually not sufficient to prevent gout flares.

(Choice B) Increased production of uric acid is commonly due to a purine-rich diet (eg, red meat, seafood), excessive alcohol intake, fructose-sweetened beverage intake, or disorders associated with increased cell turnover (eg, myeloproliferative disorders, cancers).

(Choice C) Urate-lowering agents (eg, allopurinol) are used to prevent recurrent gout but can occasionally precipitate a gout flare due to rapid declines in blood uric acid levels, which can disrupt preexisting crystal deposits and increase their immunogenicity. This patient is not taking a medication that lowers uric acid levels.

(Choice D) Patients who have malignancy associated with high tumor burdens (eg, acute lymphoblastic leukemia) can develop tumor lysis syndrome when cytotoxic chemotherapy is initiated. The massive release of nucleic acids into the circulation (from lysed cells) increases serum uric acid levels (due to catabolism of purine nucleic acids) and can precipitate gout.



levels.

(Choice D) Patients who have malignancy associated with high tumor burdens (eg, acute lymphoblastic leukemia) can develop tumor lysis syndrome when cytotoxic chemotherapy is initiated. The massive release of nucleic acids into the circulation (from lysed cells) increases serum uric acid levels (due to catabolism of purine nucleic acids) and can precipitate gout.

(Choice E) Diuretics (eg, furosemide, hydrochlorothiazide) can be associated with gout as these medications reduce urate excretion in the proximal tubule and also cause volume depletion leading to decreased renal perfusion and filtration of uric acid. This patient has a normal serum creatinine level, indicating adequate renal function.

Educational objective:

Patients undergoing solid organ transplantation are at increased risk of gout due to medications that impair renal clearance of uric acid. Cyclosporine is particularly associated with gout in the post-transplantation period due to decreased uric acid excretion.

Pharmacology

Rheumatology/Orthopedics & Sports

Gout

Subject

System

Topic

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Previous



Next



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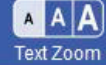
Notes



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Settings

A 70-year-old man comes to the clinic due to intermittent leg pain and difficulty walking. He describes the pain as mild-to-moderate, deep, and lasting throughout the day. The patient has a history of osteoarthritis in his hands for which he takes over-the-counter nonsteroidal anti-inflammatory drugs, but says that he never has had problems with his knees. Physical examination shows point tenderness over the right tibia. Laboratory studies show elevated serum alkaline phosphatase. Bone biopsy shows haphazardly oriented segments of lamellar bone with prominent cement lines. The initial phase of this patient's disorder involves increased activity of which of the following cell types?

- ☐ A. Chondrocytes
- ☐ B. Endothelial cells
- ☐ C. Fibroblasts
- ☐ D. Osteoblasts
- ☐ E. Osteoclasts

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Previous



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Lab Values



Notes



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Settings

A 70-year-old man comes to the clinic due to intermittent leg pain and difficulty walking. He describes the pain as mild-to-moderate, deep, and lasting throughout the day. The patient has a history of osteoarthritis in his hands for which he takes over-the-counter nonsteroidal anti-inflammatory drugs, but says that he never has had problems with his knees. Physical examination shows **point tenderness** over the right tibia. Laboratory studies show elevated serum **alkaline phosphatase**. Bone biopsy shows haphazardly oriented segments of lamellar bone with prominent **cement lines**. The initial phase of this patient's disorder involves increased activity of which of the following cell types?

- ☐ A. Chondrocytes (3%)
- ☐ B. Endothelial cells (0%)
- ☐ C. Fibroblasts (1%)
- ☐ D. Osteoblasts (26%)
- ☒ E. Osteoclasts (68%)



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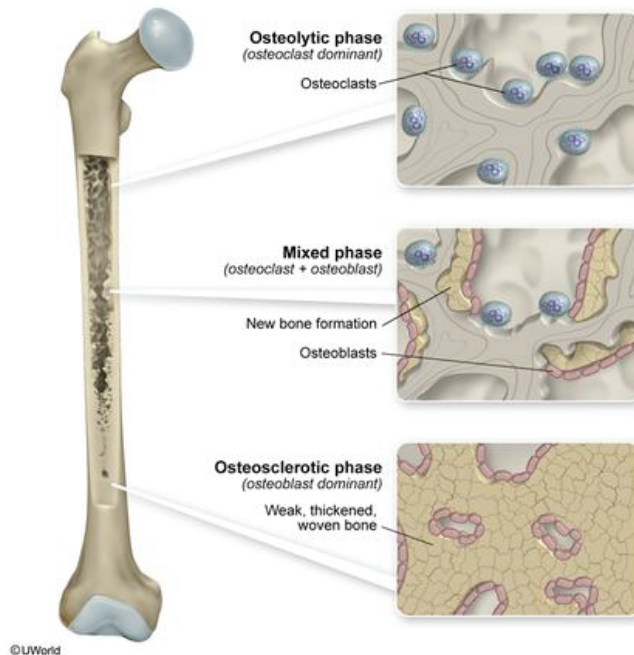
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Exhibit Display

Paget disease of bone



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Previous



Next



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This elderly patient's bone pain, increased alkaline phosphatase, and biopsy findings are characteristic of **Paget disease of bone** (PDB), a condition that results in accelerated bone remodeling with eventual bony overgrowth. The disease is thought to be caused by environmental factors and gene mutations (eg, affecting RANK, osteoprotegerin) that result in excessive RANK and NF- κ B activation. This leads to increased **osteoclast differentiation** and activity. The disease typically progresses through 3 phases:

1. **Osteolytic (osteoclast-dominant) phase** – characterized by increased numbers of osteoclasts that appear abnormally large with an excessive number of nuclei. Increased resorption activity is prominent.
2. Mixed (osteoclastic-osteoblastic) phase – defined by a rapid increase in osteoblastic bone formation with persistent osteoclastic activity. The newly made bone is abnormal, with interspersed areas of disorganized lamellar and woven bone.
3. **Osteosclerotic (osteoblast-dominant) phase** – characterized by continued osteoblastic bone formation and remodelling that result in a dense, hypovascular, **mosaic pattern** of lamellar bone with irregular, haphazardly oriented sections separated by **prominent cement lines**.

The end result is a thickened, deformed bone that is weaker than normal and prone to fracture.



Feedback



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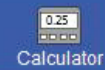
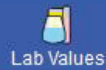
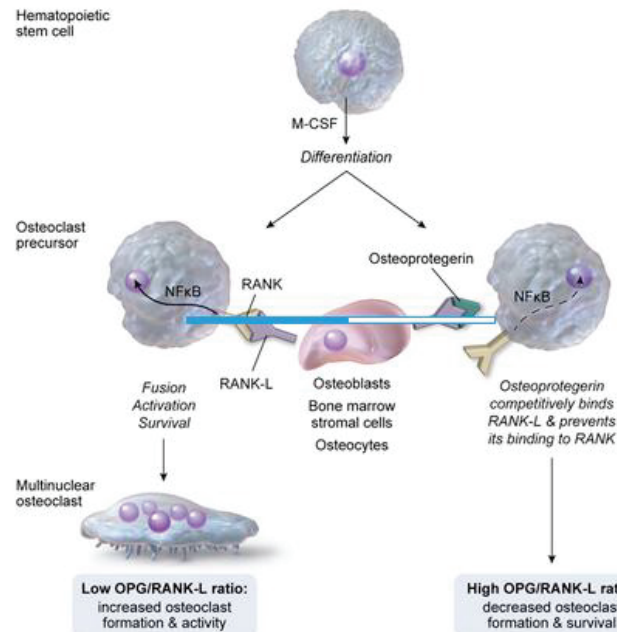
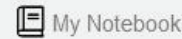
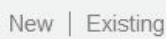
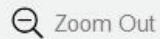
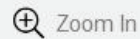


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Osteoclast differentiation



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The end result is a thickened, deformed bone that is weaker than normal and prone to fracture.

Block Time Remaining: 00:23:36

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The end result is a thickened, deformed bone that is weaker than normal and prone to fracture.

(Choice A) Chondrocytes are not involved in the pathogenesis of PDB.

(Choices B and C) In the early stages of PDB, the adjacent marrow spaces are replaced by highly vascular stromal tissue as a result of increased endothelial cell and fibroblast proliferation due to cytokines secreted by osteoclasts. The increased vascularity causes arteriovenous shunting that can result in high-output heart failure.

(Choice D) Although this patient's bone biopsy shows findings characteristic of the osteosclerotic (osteoblast-dominant) phase of Paget disease, the question is specifically asking about the **initial (osteolytic) phase** of Paget disease, where osteoclast activity is predominantly increased. Increased activity and dysregulation of osteoblasts and fibroblasts increase the risk of developing sarcomas (eg, osteosarcoma) in patients with PDB.

Educational objective:

Bone pain and elevated alkaline phosphatase level in an elderly patient can occur with osteoblast metastases and Paget disease of bone (PDB). Biopsy showing a mosaic pattern of lamellar bone is diagnostic for PDB. The initial phase in PDB is characterized by an increase in osteoclastic activity.

References



1



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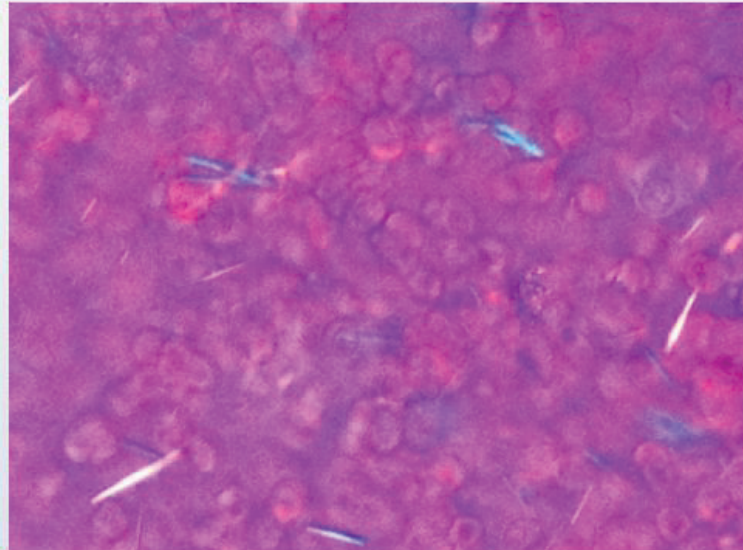


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End Block

A 55-year-old man comes to the emergency department with severe right foot pain that started suddenly in the middle of the night. He has never had such symptoms before. He has a history of diet-controlled type 2 diabetes mellitus. His BMI is 32 kg/m². Physical examination shows swelling and tenderness of the first metatarsophalangeal joint. His leukocyte count is 13,500/μL and serum creatinine is 0.8 mg/dL. Joint aspiration is performed, and synovial fluid microscopic findings are shown in the image below.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

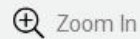
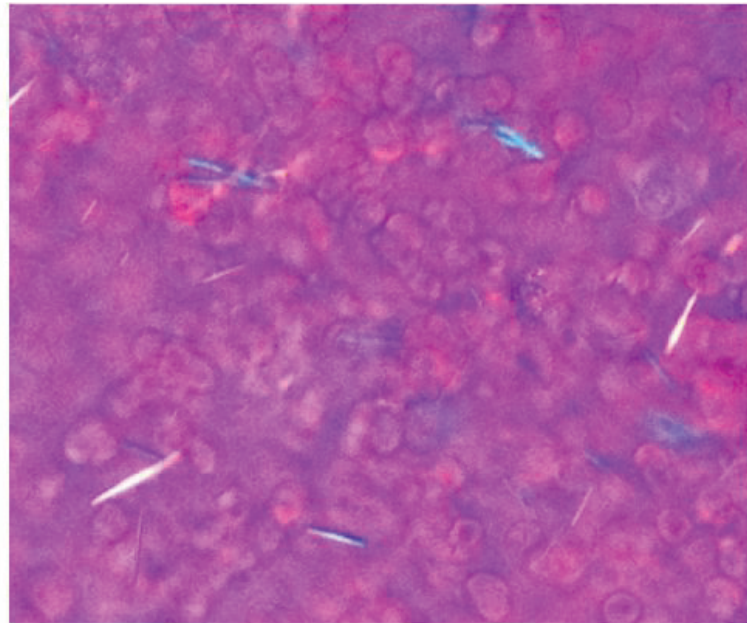


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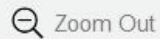


Settings

Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

My Notebook



0



Feedback



Suspend



End Block



Which of the following is the best initial treatment for this patient?

- ☐ A. Cyclooxygenase inhibitor
- ☐ B. Lipoxygenase inhibitor
- ☐ C. Oral glucocorticoid
- ☐ D. Systemic antibiotics
- ☐ E. TNF-alpha inhibitor
- ☐ F. Uricosuric agent
- ☐ G. Xanthine oxidase inhibitor

Submit



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the best initial treatment for this patient?

- ☒ A. Cyclooxygenase inhibitor (68%)
- ☐ B. Lipoxygenase inhibitor (0%)
- ☐ C. Oral glucocorticoid (9%)
- ☐ D. Systemic antibiotics (0%)
- ☐ E. TNF-alpha inhibitor (0%)
- ☐ F. Uricosuric agent (4%)
- ☐ G. Xanthine oxidase inhibitor (15%)

Correct

68%



23 secs



12/11/2020

Block Time Remaining: 00:23:59

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Suspend

End Block

Acute gouty arthritis

| | |
|-----------------------------|--|
| Signs & symptoms | <ul style="list-style-type: none">• Usually involves first metatarsophalangeal joint or knee• Swelling, erythema & exquisite tenderness• Symptoms develop rapidly over 24 hr |
| Diagnosis | <ul style="list-style-type: none">• Joint aspiration shows needle-shaped, negatively birefringent crystals |
| Treatment | <ul style="list-style-type: none">• Nonsteroidal anti-inflammatory drugs (eg, naproxen, indomethacin) preferred if no contraindications• Colchicine used as second-line therapy |

Synovial fluid analysis in this patient with acute monoarthritis shows needle-shaped, **negatively birefringent crystals** (ie, monosodium urate crystals) under polarized light, which are diagnostic for **gout**. Phagocytosis of urate crystals by neutrophils causes the release of various cytokines and inflammatory mediators that lead to further neutrophil activation and chemotaxis, resulting in a positive feedback loop that amplifies the inflammatory response.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for most patients with acute gouty arthritis. They inhibit cyclooxygenase enzymes and therefore decrease prostaglandin synthesis and



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



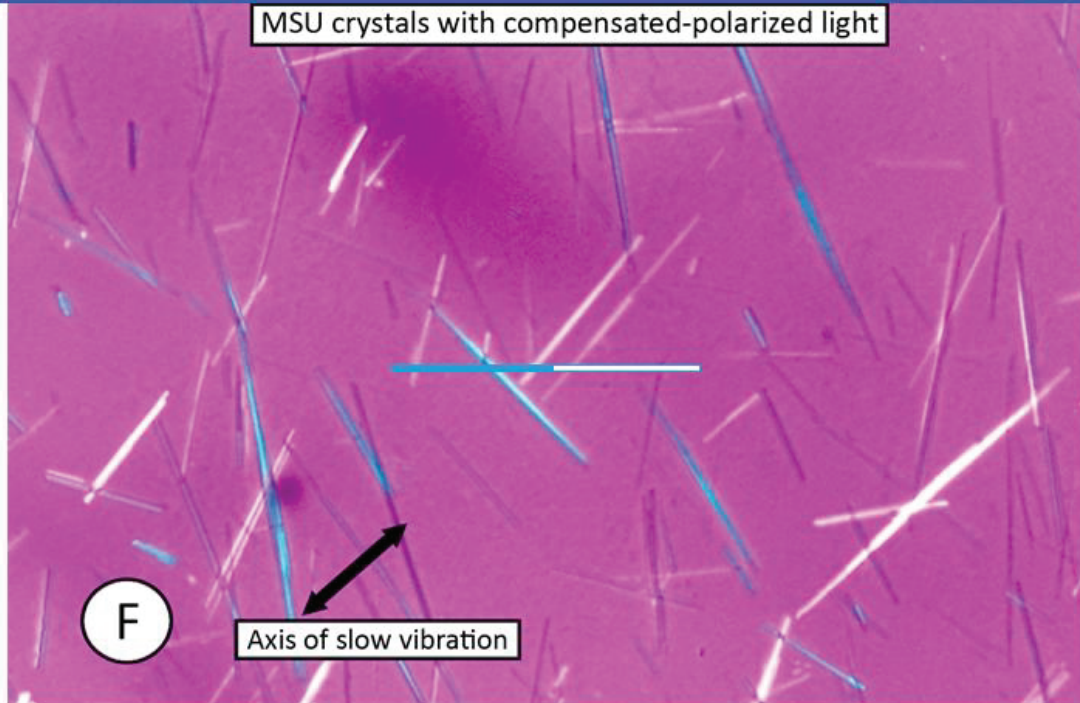
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Settings

Exhibit Display

MSU crystals with compensated-polarized light



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:23:59

TUTOR

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0

Feedback



Suspend



End Block



inflammatory response.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment for most patients with acute gouty arthritis. They inhibit cyclooxygenase enzymes and therefore decrease prostaglandin synthesis and exert a broad anti-inflammatory effect that includes inhibition of neutrophils. NSAIDs should be avoided in patients with renal and hepatic dysfunction or those at high risk for peptic ulcer.

(Choice B) Lipoxxygenase inhibitors (eg, zileuton) decrease production of pro-inflammatory leukotrienes and are indicated for treatment of asthma. Lipoxxygenase inhibitors are not useful in the treatment of acute or chronic gout.

(Choice C) Glucocorticoid therapy, either systemic or intraarticular, is used in patients with contraindications to both NSAIDs and colchicine (eg, renal dysfunction, the elderly). In addition, this patient has diabetes mellitus, and glucocorticoid use will increase his blood glucose levels.

(Choice D) Antibiotics are used in patients with acute septic arthritis. [Synovial fluid analysis](#) in septic arthritis will show bacteria and a high concentration of leukocytes.

(Choice E) TNF-alpha inhibitors (eg, infliximab, etanercept) are used as disease-modifying agents in rheumatoid arthritis.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



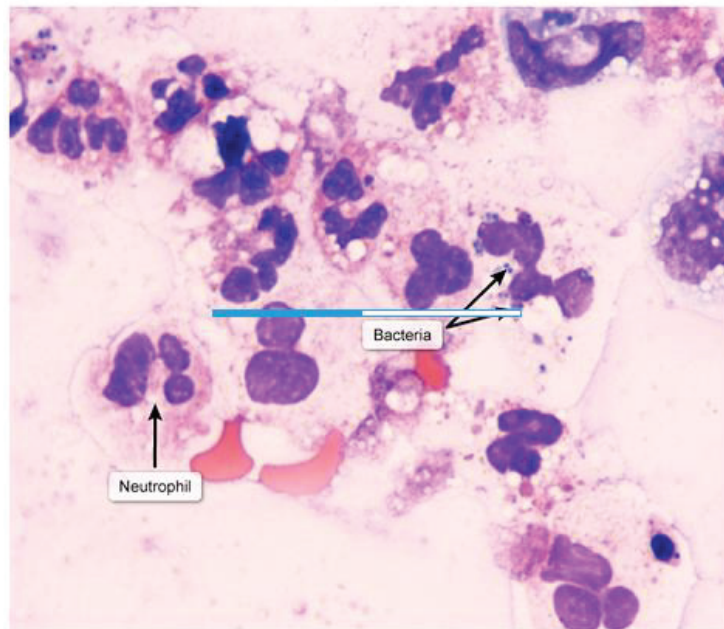
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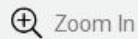
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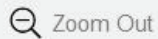
Septic arthritis



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0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice C) Glucocorticoid therapy, either systemic or intraarticular, is used in patients with contraindications to both NSAIDs and colchicine (eg, renal dysfunction, the elderly). In addition, this patient has diabetes mellitus, and glucocorticoid use will increase his blood glucose levels.

(Choice D) Antibiotics are used in patients with acute septic arthritis. [Synovial fluid analysis](#) in septic arthritis will show bacteria and a high concentration of leukocytes.

(Choice E) TNF-alpha inhibitors (eg, infliximab, etanercept) are used as disease-modifying agents in rheumatoid arthritis.

(Choices F and G) Uric acid-lowering therapy with uricosuric agents (eg, probenecid) or xanthine oxidase inhibitors (eg, allopurinol, febuxostat) is used to prevent acute attacks in patients with recurrent and progressive gouty arthritis and those with [macroscopic tophi](#). These drugs should **not** be initiated during an acute gout attack as they can exacerbate acute arthritis.

Educational objective:

Nonsteroidal anti-inflammatory drugs are the first-line treatment for acute gouty arthritis. They inhibit cyclooxygenase and therefore decrease prostaglandin synthesis and exert a broad anti-inflammatory effect that includes inhibition of neutrophils.



Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

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A 16-year-old boy comes to the office for an annual health maintenance visit. He has no medical conditions and feels well. The patient plays football for his high school team and states he is planning to increase his physical workouts to prepare for the upcoming season. He indicates that last season he was often fatigued during the second half of games, and he plans to focus on endurance training. Physical examination shows no abnormalities. Which of the following is most likely to increase in this patient's large skeletal muscle groups after a prolonged period of regular training?

- ☐ A. Anaerobic glycolytic enzymes
- ☐ B. Mitochondrial content
- ☐ C. Number of motor endplates per fiber
- ☐ D. Proportion of type II (fast-twitch) fibers
- ☐ E. Total quantity of myocytes

Submit



A 16-year-old boy comes to the office for an annual health maintenance visit. He has no medical conditions and feels well. The patient plays football for his high school team and states he is planning to increase his physical workouts to prepare for the upcoming season. He indicates that last season he was often fatigued during the second half of games, and he plans to focus on endurance training. Physical examination shows no abnormalities. Which of the following is most likely to increase in this patient's large skeletal muscle groups after a prolonged period of regular training?

- ☐ A. Anaerobic glycolytic enzymes (12%)
- ☒ B. Mitochondrial content (72%)
- ☐ C. Number of motor endplates per fiber (2%)
- ☐ D. Proportion of type II (fast-twitch) fibers (8%)
- ☐ E. Total quantity of myocytes (3%)

Correct

72%
Answered correctly01 min
Time Spent12/31/2020
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Block Time Remaining: 00:24:59

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Feedback



Suspend



End Block

Muscle fiber characteristics

| | Type I (slow twitch) | Type II (fast twitch) |
|------------------------------|-------------------------------|--|
| Action | Sustained force (eg, posture) | Rapid bursts (eg, heavy weightlifting) |
| Activity type | Endurance (aerobic) | Resistance (anaerobic) |
| Force generated | Low | High |
| Resistance to fatigue | High | Low |
| Lipid content | High | Low |
| Glycogen content | Low | High |
| Mitochondrial content | High | Low |
| Energy metabolism | Oxidative | Glycolytic |
| Color | Red (high myoglobin) | Pale red/white (low myoglobin) |
| Prototype | Soleus | Triceps |

Skeletal muscle fibers (or myocytes) are categorized into 2 major types based on the magnitude and

Skeletal muscle fibers (or myocytes) are categorized into 2 major types based on the magnitude and sustainability of contraction force they generate and their predominant method of energy production.

Type I fibers (slow-twitch fibers) specialize in **stamina** (fatigue resistance) but can generate only relatively **low force** per contraction. These fibers primarily use **oxidative phosphorylation** (OP) to allow for sustained and efficient production of ATP. Therefore, they have a **high content** of **lipids** (fatty acids are a primary energy source for OP), **myoglobin** (to supply oxygen), and **mitochondria** (the cellular location of OP). The high myoglobin content gives these fibers a red color.

Type II fibers (fast-twitch fibers) primarily specialize in rapid bursts of strength; they generate **high force** per contraction but **quickly fatigue**. These fibers produce ATP primarily via **anaerobic glycolysis** and have **high glycogen** levels. Therefore, they have low quantities of mitochondria and myoglobin (giving them a pale red or white color).

Targeted physical training stimulates specific phenotypic adaptations in skeletal muscle fibers to improve skeletal muscle function. **Endurance training** (eg, distance running, sustained light-to-moderate weightlifting) **promotes** the characteristics of **type I fibers** (eg, increased size and quantity of mitochondria) and also increases capillary density. In contrast, resistance training (eg, heavy weightlifting) amplifies the characteristics of type II fibers while also stimulating increased muscle mass.



amplifies the characteristics of type II fibers while also stimulating increased muscle mass.

(Choice A) Anaerobic glycolytic enzymes will decrease and aerobic oxidative enzymes will increase with endurance training.

(Choice C) Muscle fibers are arranged into a motor unit, with each unit innervated by a single motor neuron and endplate. Although the size and metabolic characteristics of muscle fibers change with training, the number of muscle fibers within a motor unit or endplates per fiber does not change.

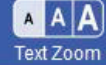
(Choices D and E) Endurance training amplifies the phenotypic characteristics of existing type I fibers; however, the total quantity of muscle fibers (myocytes) or the proportion of each type of muscle fiber does not significantly change with training.

Educational objective:

Type I muscle fibers (slow-twitch or red fibers) primarily use oxidative phosphorylation and contain high quantities of lipids, myoglobin, and mitochondria. They specialize in sustained, low force contraction, and their function is amplified by endurance training. Type II muscle fibers (fast-twitch or white fibers) primarily use glycolysis and specialize in rapid bursts of high force contraction. Their function is amplified by resistance training.

References





A 27-year-old man comes to the emergency department due to several hours of right foot pain and swelling. The patient says he was working in his barn last night and stepped on an old nail. This morning, he awoke with pain near the injury site. It has increased throughout the day and is accompanied by progressive swelling. The patient has no chronic medical conditions and takes no medications. Temperature is 38.1 C (100.6 F), blood pressure is 135/75 mm Hg, and pulse is 95/min. The right foot is swollen with some erythema around the injury site. Radiographic imaging reveals gas in the tissues. Surgical exploration shows extensive tissue necrosis. Culture from the site reveals gram-positive rods. Which of the following best describes the mechanism of action of the toxin responsible for the necrotic effects seen in this patient?

- ☐ A. Actin depolymerization
- ☐ B. Carbohydrate degradation
- ☐ C. Elongation factor ribosylation
- ☐ D. Phospholipid splitting
- ☐ E. Plasminogen activation



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- ☐ B. Carbohydrate degradation
- ☐ C. Elongation factor ribosylation
- ☐ D. Phospholipid splitting
- ☐ E. Plasminogen activation
- ☐ F. Presynaptic acetylcholine release inhibition
- ☐ G. T-cell hyperstimulation

Submit

Block Time Remaining: 00:25:05

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Suspend

End Block

progressive swelling. The patient has no chronic medical conditions and takes no medications.

Temperature is 38.1 C (100.6 F), blood pressure is 135/75 mm Hg, and pulse is 95/min. The right foot is swollen with some erythema around the injury site. Radiographic imaging reveals gas in the tissues.

Surgical exploration shows extensive tissue necrosis. Culture from the site reveals gram-positive rods.

Which of the following best describes the mechanism of action of the toxin responsible for the necrotic effects seen in this patient?

- ☐ A. Actin depolymerization (7%)
- ☐ B. Carbohydrate degradation (5%)
- ☐ C. Elongation factor ribosylation (8%)
- ☒ D. Phospholipid splitting (66%)
- ☐ E. Plasminogen activation (1%)
- ☐ F. Presynaptic acetylcholine release inhibition (9%)
- ☐ G. T-cell hyperstimulation (2%)



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Mechanism of action of bacterial toxins

| Organism | Toxin | Microbiology |
|---|------------------|--|
| <i>Corynebacterium diphtheriae</i> | Diphtheria toxin | Inactivates EF-2 via ribosylation → blocks host cell protein synthesis |
| <i>Pseudomonas aeruginosa</i> | Exotoxin A | Inactivates EF-2 via ribosylation → blocks host cell protein synthesis |
| <i>Staphylococcus aureus</i> | Enterotoxin | Superantigen → acts locally in upper GI tract → vomiting |
| | TSS toxin | Superantigen → stimulates T cells → widespread cytokine release & shock |
| <i>Clostridioides difficile</i> | Cytotoxin B | Actin depolymerization → mucosal cell death, necrosis & pseudomembrane formation |
| <i>Clostridium botulinum</i> | Botulinum toxin | Blocks presynaptic release of acetylcholine at the neuromuscular junction → flaccid paralysis |
| <i>Bordetella</i> | Pertussis | Disinhibits adenylate cyclase via Gi ADP-ribosylation → increases cAMP production in the host cell → increases |

Block Time Remaining: 00:26:48

TUTOR

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Feedback

Suspend

End Block

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|---|-----------------|---|
| <i>Bordetella pertussis</i> | Pertussis toxin | increases cAMP production in the host cell → increases histamine sensitivity & phagocyte dysfunction |
| <i>Vibrio cholerae</i> | Cholera toxin | Activates adenylate cyclase via Gs ADP-ribosylation → increases cAMP production in host cell → secretory diarrhea, dehydration & electrolyte imbalances |
| <i>Clostridium perfringens</i> | Alpha toxin | Phospholipase C mimetic → splits host phospholipids → cell lysis & tissue necrosis |
| EF-2 = elongation factor 2; GI = gastrointestinal; TSS = toxic shock syndrome. | | |

This patient has rapidly progressive pain, swelling, and gas/necrosis at the site of a penetrating foot injury, raising strong suspicion for ***Clostridium perfringens*** infection. *C perfringens* is an obligate anaerobic, spore-forming, **gram-positive rod** found in soil. Most cases develop following the introduction of spores into tissue during **penetrating injury** (eg, knife wound, puncture wound); significant vascular damage is generally required to create the **anaerobic environment** necessary for vegetative bacterial proliferation.

C perfringens classically causes **gas gangrene** (eg, necrosis, gas in tissue) **within hours** of infection.

This is primarily mediated by the generation of **alpha toxin** (lecithinase), a potent phospholipase C mimetic



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

C perfringens classically causes **gas gangrene** (eg, necrosis, gas in tissue) **within hours** of infection.

This is primarily mediated by the generation of **alpha toxin** (lecithinase), a potent phospholipase C mimetic that **splits host phospholipids**. This compound hydrolyzes lecithin-containing lipoprotein complexes in cell membranes, which causes cell lysis, tissue necrosis, and edema. It also mediates intravascular aggregations of platelets, neutrophils, and fibrin, which results in vascular occlusion and further promotes the anaerobic environment required for bacterial proliferation. Although *C perfringens* produces a vast array of other cytotoxins, alpha toxin is thought to mediate its most devastating effects.

C perfringens uses **carbohydrates** for energy; its rapid metabolism of muscle tissue carbohydrates produces significant amounts of **gas**, which can be seen on plain radiographs or CT scans (**Choice B**).

(**Choice A**) Actin depolymerization is mediated by *Clostridioides* (formerly *Clostridium*) *difficile* cytotoxin B, which primarily causes infectious diarrhea.

(**Choice C**) Inactivation of elongation factor 2 through ribosylation is the mechanism of action for diphtheria toxin. Cutaneous diphtheria is generally marked by nonhealing ulcers; it does not typically cause rapid-onset necrosis and gas formation.

(**Choice E**) Plasminogen activators such as streptokinase, urokinase, and tissue plasminogen activator



1



Feedback



Suspend



End Block

onset necrosis and gas formation.

(Choice E) Plasminogen activators such as streptokinase, urokinase, and tissue plasminogen activator convert plasminogen to plasmin. Of these 3 enzymes, only streptokinase, an exotoxin released by *Streptococcus pyogenes* (group A *Streptococcus*), is a bacterial product. Streptococcal skin infection is usually marked by spreading, nonpurulent cellulitis, not gas gangrene.

(Choice F) Inhibition of presynaptic acetylcholine release is the mechanism of action of botulinum toxin, which primarily causes cranial neuropathy and descending paralysis.

(Choice G) Certain *Staphylococcus aureus*-produced toxins act as superantigens by hyperstimulating T cells and causing massive cytokine production. Examples include enterotoxin, which causes food poisoning, and toxic shock syndrome toxin. *S aureus* can cause purulent cellulitis, but rapid-onset gas gangrene is atypical.

Educational objective:

Lecithinase (alpha toxin) is the main toxin produced by *Clostridium perfringens*. It degrades lecithin, a component of cellular phospholipid membranes, which leads to membrane destruction, cell death, and widespread necrosis and hemolysis.



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 52-year-old man comes to the office due to right shoulder pain. He is an avid golfer but has been unable to play for the past 3 months due to the pain. Lately, it has started to interfere with his daily activities, such as getting dressed. An MRI shows thickening and calcification of the supraspinatus tendon. Which of the following shoulder actions is most likely to provoke pain in this patient?

- ☐ A. Abduction
- ☐ B. Adduction
- ☐ C. Extension
- ☐ D. Flexion
- ☐ E. Internal rotation

Submit

0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

A 52-year-old man comes to the office due to right shoulder pain. He is an avid golfer but has been unable to play for the past 3 months due to the pain. Lately, it has started to interfere with his daily activities, such as getting dressed. An MRI shows thickening and calcification of the supraspinatus tendon. Which of the following shoulder actions is most likely to provoke pain in this patient?

- ☒ A. Abduction (84%)
- ☐ B. Adduction (3%)
- ☐ C. Extension (2%)
- ☐ D. Flexion (2%)
- ☐ E. Internal rotation (7%)

Correct

 84%
Answered correctly 01 min, 29 secs
Time Spent 01/07/2021
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Explanation

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Feedback



Suspend



End Block

Rotator cuff muscles

| Muscle | Origin on scapula | Attachment on humerus | Function on arm | Innervation |
|---------------|--------------------|---|------------------------------------|---------------------------------|
| Supraspinatus | Supraspinous fossa | Superior aspect of greater tubercle | Abduction (primarily $<15^\circ$) | Suprascapular nerve |
| Infraspinatus | Infraspinous fossa | Posterolateral aspect of greater tubercle | External rotation | Suprascapular nerve |
| Teres minor | Lateral border | Posterolateral aspect of greater tubercle | Adduction & external rotation | Axillary nerve |
| Subscapularis | Subscapular fossa | Lesser tubercle | Adduction & internal rotation | Upper & lower subscapular nerve |

The **rotator cuff** is made up of the tendons of the supraspinatus, infraspinatus, subscapularis, and teres minor muscles. These tendons, along with the tendon of the long head of the biceps brachii muscle and the ligaments of the glenohumeral joint, contribute to shoulder stability.



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

minor muscles. These tendons, along with the tendon of the long head of the biceps brachii muscle and the ligaments of the glenohumeral joint, contribute to shoulder stability.

In rotator cuff syndrome, the most commonly injured tendon is the supraspinatus as this tendon is prone to repeated impingement trauma between the humeral head and the **acromion**, especially in abduction. The supraspinatus is primarily an abductor of the arm; it originates in the supraspinous fossa of the scapula and inserts on the superior portion of the head of the humerus. Therefore, supraspinatus tendinopathy is associated with pain on abduction of the humerus, especially resisted active abduction.

(Choice B) Adduction of the humerus is accomplished by several muscles, including the latissimus dorsi, pectoralis major, coracobrachialis, subscapularis, and teres major and minor.

(Choice C) Extension of the humerus is accomplished primarily by the latissimus dorsi, posterior deltoid, and teres major.

(Choice D) Flexion of the humerus at the shoulder is accomplished primarily by the pectoralis major, coracobrachialis, biceps brachii, and anterior deltoid.

(Choice E) Internal rotation of the humerus is accomplished by the subscapularis muscle, which originates in the subscapular fossa and inserts on the lesser tubercle of the head of the humerus with contribution



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

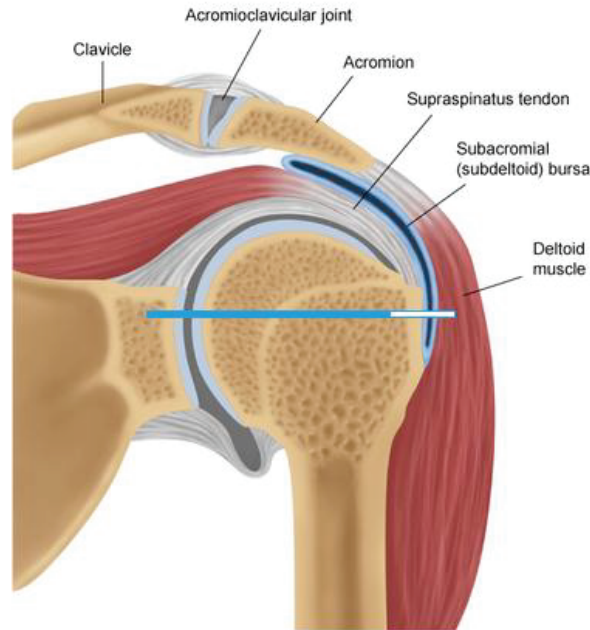
Reverse Color

Text Zoom

Settings

Exhibit Display

Rotator cuff



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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(Choice D) Flexion of the humerus at the shoulder is accomplished primarily by the pectoralis major, coracobrachialis, biceps brachii, and anterior deltoid.

(Choice E) Internal rotation of the humerus is accomplished by the subscapularis muscle, which originates in the subscapular fossa and inserts on the lesser tubercle of the head of the humerus with contribution from the teres major, pectoralis major, anterior deltoid, and latissimus dorsi.

Educational objective:

The most commonly injured structure in rotator cuff syndrome is the tendon of the supraspinatus muscle. Because the supraspinatus is an abductor of the humerus, injury to its tendon causes pain on abduction of the arm.

Anatomy

Rheumatology/Orthopedics & Sports

Rotator cuff

Subject

System

Topic





A 52-year-old woman comes to the office due to pain in the right knee for the past several months. The pain is typically better in the morning but worsens by the end of the day. There is no history of trauma to the joint. Medical history is significant for hypertension, type 2 diabetes mellitus, and hypercholesterolemia. The patient is a lifetime nonsmoker. She works as an office clerk. Family history is significant for stroke in her mother and gout in her father. Temperature is 37.2 C (99 F), blood pressure is 145/95 mm Hg, and pulse is 90/min. BMI is 37 kg/m². Physical examination shows crepitation on flexion and extension of the right knee; range of motion is otherwise normal, and there is no swelling, warmth, or redness. Which of the following pathologic processes is most likely occurring in this patient's knee joint?

- ☐ A. Calcium pyrophosphate crystal deposition
- ☐ B. Fissuring and flaking of articular cartilage
- ☐ C. Iron deposition in cartilage
- ☐ D. Synovial cell hyperplasia
- ☐ E. Virus-induced synovial inflammation





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

pain is typically better in the morning but worsens by the end of the day. There is no history of trauma to the joint. Medical history is significant for hypertension, type 2 diabetes mellitus, and hypercholesterolemia. The patient is a lifetime nonsmoker. She works as an office clerk. Family history is significant for stroke in her mother and gout in her father. Temperature is 37.2 C (99 F), blood pressure is 145/95 mm Hg, and pulse is 90/min. BMI is 37 kg/m². Physical examination shows crepitation on flexion and extension of the right knee; range of motion is otherwise normal, and there is no swelling, warmth, or redness. Which of the following pathologic processes is most likely occurring in this patient's knee joint?

- ☐ A. Calcium pyrophosphate crystal deposition (8%)
- ☒ B. Fissuring and flaking of articular cartilage (84%)
- ☐ C. Iron deposition in cartilage (0%)
- ☐ D. Synovial cell hyperplasia (6%)
- ☐ E. Virus-induced synovial inflammation (0%)

Correct

84%



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03/01/2021

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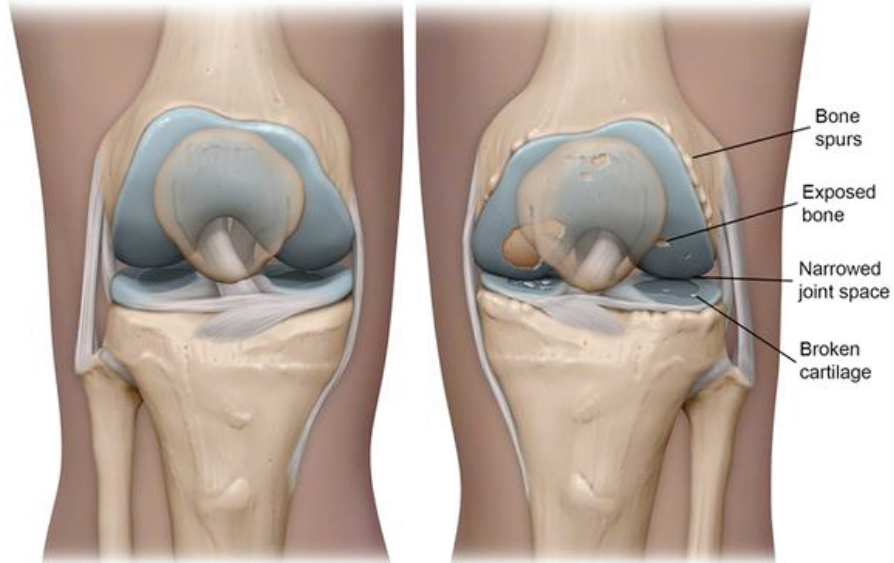
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Exhibit Display

Osteoarthritis

Normal

Osteoarthritis



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Previous



Next



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This patient has **chronic knee pain** associated with **crepitus**, which is consistent with **osteoarthritis** (the most common form of arthritis). Besides the knees, osteoarthritis also commonly affects the hips, lumbar spine, and distal joints of the hands. Patients typically have pain that worsens with activity and is relieved by rest. Osteoarthritis typically progresses with age and is accelerated in patients with prior joint injury or excessive mechanical stresses (eg, **obesity**, joint deformities).

Osteoarthritis is characterized by progressive **fissuring, flaking, and erosion** (fibrillation) of **articular cartilage**. The etiology is multifactorial, with excessive biomechanical stress and **increased intraarticular metalloproteinase activity** as the major contributors to cartilage destruction. Although a number of proinflammatory mediators (eg, IL-6, macrophage chemotactic protein-1) have been linked to osteoarthritis, overt signs of synovitis (eg, redness, warmth) are less prominent than in the classic inflammatory arthritic disorders (eg, gout). Effusions, if present, are often small.

(Choice A) Calcium pyrophosphate deposition disease presents with an acute inflammatory arthritis resembling gout (ie, pseudogout). Although this disorder is common in the knee, chronic arthritis without signs of acute synovitis is more consistent with osteoarthritis.

(Choice C) Hemochromatosis can cause deposition of iron salts within the synovium and joint space,



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(Choice C) Hemochromatosis can cause deposition of iron salts within the synovium and joint space, which can lead to a chronic arthritis resembling osteoarthritis. Although hereditary hemochromatosis is associated with diabetes mellitus, this patient lacks other characteristic findings (eg, skin pigmentation, liver dysfunction, cardiac enlargement); in addition, osteoarthritis is a much more common cause of arthritis in the general population.

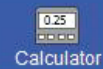
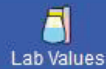
(Choice D) Rheumatoid arthritis is an inflammatory arthritis associated with synovial hyperplasia. It most commonly affects the proximal interphalangeal (PIP), metacarpophalangeal (MCP), wrist, knee, and ankle joints. However, patients typically have symmetric joint involvement and prolonged morning stiffness.

(Choice E) Parvovirus B19 presents in adults as a nonspecific flulike illness, often followed by a symmetric arthritis most commonly affecting the hands. Symptoms are acute and resolve within a few weeks.

Educational objective:

Osteoarthritis is characterized by progressive fissuring and erosion of articular cartilage. Risk factors include advancing age, obesity, joint trauma, and repetitive stress. Patients may have mild effusion and crepitus on physical examination, but signs of synovitis (eg, redness, warmth) are less prominent than in the classic inflammatory arthritic disorders.

References



A 16-year-old high school quarterback comes to the office due to left shoulder pain. One week ago, he suffered an injury during a football game. The patient was running with the football when another player tackled him to the ground, causing him to land directly on the posterior aspect of his left shoulder. He developed severe pain immediately and did not return to the game. The patient has had persistent shoulder pain since the injury despite using ice and over-the-counter ibuprofen. He has been unable to resume playing football due to pain and weakness in his shoulder. On examination, there is diffuse bruising over the posterior aspect of the left shoulder. Abduction of the left arm is normal, but external rotation against resistance is weak and painful. Which of the following muscles is most likely injured?

- ☐ A. Biceps brachii
- ☐ B. Infraspinatus
- ☐ C. Subscapularis
- ☐ D. Supraspinatus
- ☐ E. Teres major
- ☐ F. Trapezius





tackled him to the ground, causing him to land directly on the posterior aspect of his left shoulder. He developed severe pain immediately and did not return to the game. The patient has had persistent shoulder pain since the injury despite using ice and over-the-counter ibuprofen. He has been unable to resume playing football due to pain and weakness in his shoulder. On examination, there is diffuse bruising over the posterior aspect of the left shoulder. Abduction of the left arm is normal, but external rotation against resistance is weak and painful. Which of the following muscles is most likely injured?

- ☐ A. Biceps brachii (1%)
- ☒ B. Infraspinatus (59%)
- ☐ C. Subscapularis (14%)
- ☐ D. Supraspinatus (9%)
- ☐ E. Teres major (11%)
- ☐ F. Trapezius (3%)

Correct

59%

01 min, 47 secs

02/19/2021

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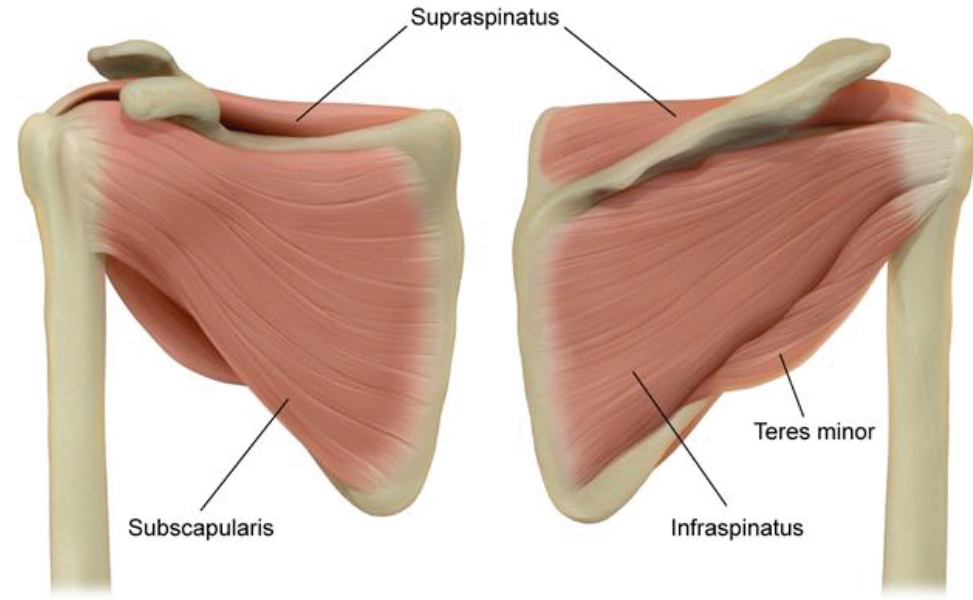
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Rotator cuff muscles

Anterior view

Posterior view



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This patient's shoulder pain and weak, painful external rotation against resistance with preserved abduction



This patient's shoulder pain and weak, painful external rotation against resistance with preserved abduction are characteristic of an **infrapinatus injury**. The **rotator cuff muscles** all attach to the humeral head and stabilize the shoulder joint, in addition to moving the arm at the shoulder. A fall onto the shoulder is a common mechanism for rotator cuff injury, resulting in acute shoulder pain and characteristic weakness depending on which muscle is involved:

- The supraspinatus inserts onto the superior aspect of the greater tubercle and abducts the arm **(Choice D)**.
- The **infrapinatus** inserts onto the posterolateral aspect of the greater tubercle and **externally rotates** the arm.
- The teres minor inserts onto the posterolateral aspect of the greater tubercle and helps with adduction and external rotation of the arm.
- The subscapularis inserts onto the lesser tubercle on the anterior aspect of the humerus and helps with adduction and internal rotation of the arm **(Choice C)**.

(Choice A) The biceps brachii is a 2-headed muscle that originates from the scapula and converges onto a single insertion point on the upper forearm. It is responsible for flexion at the elbow and forearm supination. Biceps injury can cause shoulder pain but would not affect external rotation of the arm at the



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This patient's should
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stabilize the should
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depending on which

- The **supraspinatus** **(Choice D)**.
- The **infraspinatus** **rotates** the arm.
- The **teres minor** and **external rotator**.
- The **subscapularis** with **adduction**.

(Choice A) The biceps brachii muscle is a single insertion point for the humerus in supination. Biceps

| Rotator cuff muscles | | | | |
|----------------------|--------------------|---|-------------------------------|---------------------------------|
| Muscle | Origin on scapula | Attachment on humerus | Function on arm | Innervation |
| Supraspinatus | Supraspinous fossa | Superior aspect of greater tubercle | Abduction (primarily <15°) | Suprascapular nerve |
| Infraspinatus | Infraspinous fossa | Posterolateral aspect of greater tubercle | External rotation | Suprascapular nerve |
| Teres minor | Lateral border | Posterolateral aspect of greater tubercle | Adduction & external rotation | Axillary nerve |
| Subscapularis | Subscapular fossa | Lesser tubercle | Adduction & internal rotation | Upper & lower subscapular nerve |



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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(Choice A) The biceps brachii is a 2-headed muscle that originates from the scapula and converges onto a single insertion point on the upper forearm. It is responsible for flexion at the elbow and forearm supination. Biceps injury can cause shoulder pain but would not affect external rotation of the arm at the shoulder.

(Choice E) Unlike the teres minor, the **teres major** is not a rotator cuff muscle. It arises from the inferior scapula and inserts below the humeral head onto the anterior aspect of the humerus. It assists with humeral extension (when the arm is flexed) and internal rotation of the arm at the shoulder.

(Choice F) The **trapezius** originates from the occipital bone and spinous processes of the cervical and thoracic vertebrae and inserts onto the scapula and clavicle. It helps move and rotate the scapula. Trapezius injury would cause difficulty with arm abduction and adduction, but would not affect external rotation of the humerus.

Educational objective:

The rotator cuff muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) all insert onto the humeral head, allowing them to stabilize the shoulder joint and move the arm at the shoulder. An infraspinatus injury would result in shoulder pain and weak, painful external rotation of the arm against resistance.



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

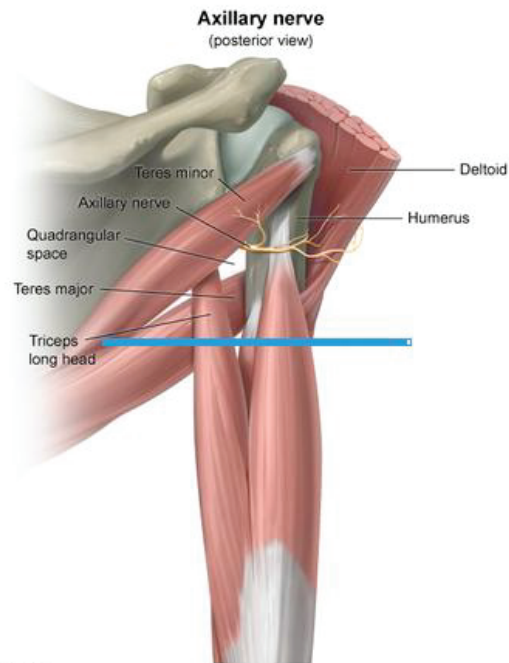
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Settings

(Choice A) The biceps brachii is a 2-headed muscle that originates from the scapula and converges onto

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Reset

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My Notebook





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

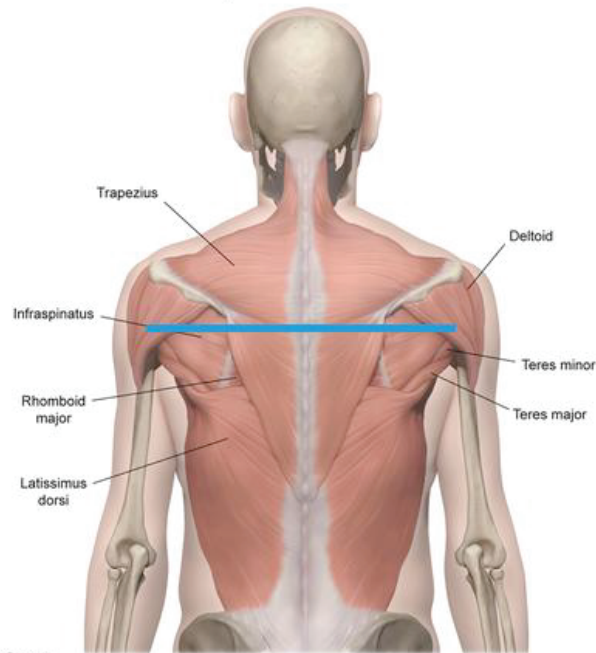
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(Choice A) The biceps brachii is a 2-headed muscle that originates from the scapula and converges onto

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Superficial back muscles



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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 3-year-old boy is brought to the office by his parents. They say that the child cannot keep up with his cousin, who is the same age. The boy climbs up from a squat by using his hands to push off the ground and his lower extremities. His calves appear enlarged on physical examination. This patient's condition is most likely associated with which of the following?

- ☐ A. Endomysial inflammatory infiltration
- ☐ B. Endoneural inflammatory infiltration
- ☒ C. Mutation affecting a muscle ion channel protein
- ☐ D. Mutation affecting a myelin protein
- ☐ E. Mutation affecting a sarcolemma-cytoskeleton linker protein
- ☐ F. Mutation affecting a sarcomere protein

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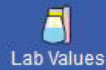
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A 3-year-old boy is brought to the office by his parents. They say that the child cannot keep up with his cousin, who is the same age. The boy climbs up from a squat by using his hands to push off the ground and his lower extremities. His calves appear enlarged on physical examination. This patient's condition is most likely associated with which of the following?

- ☐ A. Endomysial inflammatory infiltration (3%)
- ☐ B. Endoneural inflammatory infiltration (0%)
- ☐ C. Mutation affecting a muscle ion channel protein (3%)
- ☐ D. Mutation affecting a myelin protein (3%)
- ☒ E. Mutation affecting a sarcolemma-cytoskeleton linker protein (74%)
- ☐ F. Mutation affecting a sarcomere protein (14%)

Correct



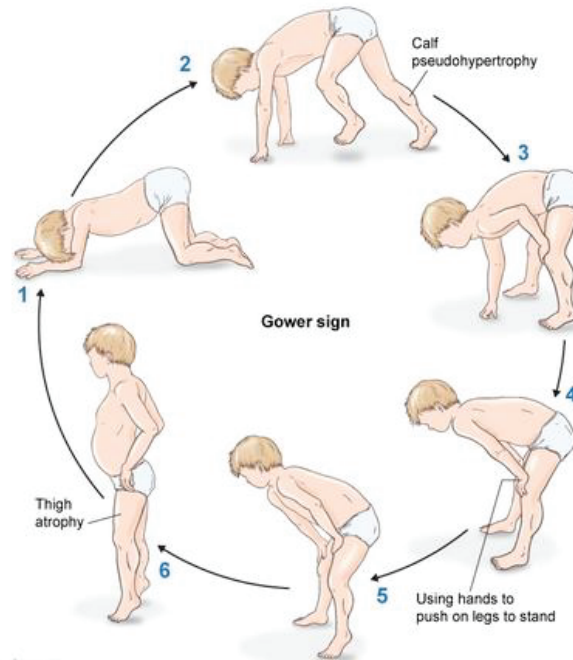
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My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Muscular dystrophy is a term that applies to the various diseases that manifest with progressive muscular weakness. **Deletions** of the dystrophin gene that encodes the **dystrophin** protein on X chromosome p21 are the most common mutation in **Duchenne muscular dystrophy** (DMD) and Becker muscular dystrophy (BMD). Deletions that are not a multiple of 3 change the reading frame, causing a **frameshift mutation**, which results in a nonfunctional protein and severe clinical manifestations (DMD). In contrast, deletions that are a multiple of 3 base pairs preserve the reading frame, resulting in a truncated but functional protein and a milder clinical phenotype (BMD).

Dystrophin is a structural component of skeletal muscle fibers that provides mechanical stability to the sarcolemma. It **links** a component of the **cytoskeleton** (actin) to **transmembrane proteins** (α - and β -dystrophiglycans) that are connected to the extracellular matrix. Loss of dystrophin results in cellular injury (myonecrosis). On light microscopy, there is segmental degeneration and regeneration of the myofibers with marked variation in size (both atrophic and hypertrophic fibers). Over time, the muscle tissue undergoes progressive fatty replacement.

On clinical examination, the presence of **Gowers sign** and calf enlargement in a boy age 2-5 is classic for DMD. Calf hypertrophy allows affected children to overcome proximal muscle weakness, but it is later replaced by fat and connective tissue (**pseudohypertrophy**). The Gowers sign involves the use of one's



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

replaced by fat and connective tissue (pseudohypertrophy). The Gowers sign involves the use of one's hands to rise from a squat or from a chair to compensate for proximal muscle weakness.

(Choice A) Endomysial inflammatory infiltration is found on muscle biopsy in polymyositis.

Dermatomyositis is associated with perifascicular inflammation. Both diseases cause proximal muscle weakness but not distal muscle hypertrophy.

(Choice B) Endoneural inflammatory infiltration is characteristic of Guillain-Barré syndrome, which classically manifests as ascending flaccid paralysis and hyporeflexia.

(Choice C) Examples of ion channel myopathies include hyper- and hypokalemic periodic paralysis, which present with episodic, painless muscle weakness.

(Choice D) Charcot-Marie-Tooth disease is due to mutation of the genes responsible for myelin synthesis. Affected patients frequently present with distal muscle weakness, sensory loss, and atrophy of the calf muscles (producing the characteristic stork leg deformity).

(Choice F) Mutations involving sarcomere proteins are responsible for hypertrophic cardiomyopathy and certain forms of familial dilated cardiomyopathy.

Educational objective:

Duchenne muscular dystrophy is an X-linked recessive myopathy that manifests with proximal muscle





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

classically manifests as ascending flaccid paralysis and hyporeflexia.

(Choice C) Examples of ion channel myopathies include hyper- and hypokalemic periodic paralysis, which present with episodic, painless muscle weakness.

(Choice D) Charcot-Marie-Tooth disease is due to mutation of the genes responsible for myelin synthesis. Affected patients frequently present with distal muscle weakness, sensory loss, and atrophy of the calf muscles (producing the characteristic stork leg deformity).

(Choice F) Mutations involving sarcomere proteins are responsible for hypertrophic cardiomyopathy and certain forms of familial dilated cardiomyopathy.

Educational objective:

Duchenne muscular dystrophy is an X-linked recessive myopathy that manifests with proximal muscle weakness and enlargement of the calf muscles in boys age 2-5. It most often results from frameshift deletions affecting the dystrophin gene. Dystrophin provides a stabilizing interaction between the sarcolemma and the intracellular contraction apparatus, and disruption of the protein results in membrane damage and myonecrosis.

References

- [Muscle disease.](#)



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 67-year-old man comes to the office due to a persistent headache and pain in the jaw when chewing food. For the past 2 months, he has been unable to eat "tough foods like steak because the pain makes it take too long to chew them." Medical history is notable for hypertension, type 2 diabetes mellitus, and hyperlipidemia. Blood pressure is 130/70 mm Hg, and pulse is 76/min and regular. Physical examination is unremarkable. Appropriate therapy is immediately started, and an arterial biopsy is performed. Histopathology shows multinuclear giant cells and internal elastic membrane fragmentation. Prompt institution of therapy in this patient most likely reduces the risk of which of the following complications?

- ☐ A. Angle-closure glaucoma
- ☐ B. Ischemic optic neuropathy
- ☐ C. Proliferative retinopathy
- ☐ D. Retinal detachment
- ☐ E. Retinal vein occlusion
- ☐ F. Vitreous hemorrhage



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

food. For the past 2 months, he has been unable to eat "tough foods like steak because the pain makes it take too long to chew them." Medical history is notable for hypertension, type 2 diabetes mellitus, and hyperlipidemia. Blood pressure is 130/70 mm Hg, and pulse is 76/min and regular. Physical examination is unremarkable. Appropriate therapy is immediately started, and an arterial biopsy is performed. Histopathology shows multinuclear giant cells and internal elastic membrane fragmentation. Prompt institution of therapy in this patient most likely reduces the risk of which of the following complications?

- ☐ A. Angle-closure glaucoma (1%)
- ☒ B. Ischemic optic neuropathy (75%)
- ☐ C. Proliferative retinopathy (5%)
- ☐ D. Retinal detachment (5%)
- ☐ E. Retinal vein occlusion (9%)
- ☐ F. Vitreous hemorrhage (2%)

Correct

75%
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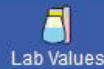
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Giant cell arteritis

| | |
|------------------|--|
| Symptoms | <ul style="list-style-type: none">• Systemic: fever, fatigue, malaise, weight loss• Headache• Jaw claudication• Visual disturbances (eg, ischemic optic neuropathy)• Polymyalgia rheumatica |
| Diagnosis | <ul style="list-style-type: none">• Elevated erythrocyte sedimentation rate & C-reactive protein• Temporal artery biopsy: intimal thickening, elastic lamina fragmentation, multinucleated giant cells |
| Treatment | <ul style="list-style-type: none">• Glucocorticoids |

This patient with headache and jaw claudication has typical symptoms of **giant cell (temporal) arteritis** (GCA). GCA occurs almost exclusively in individuals age >50 and is characterized by **granulomatous inflammation** of the media with **fragmentation of the internal elastic lamina**, primarily in the arteries of the head and neck. About half of patients with GCA also have polymyalgia rheumatica, which presents with pain and stiffness in the shoulders and hips.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

with pain and stiffness in the shoulders and hips.

Inflammatory markers (ie, erythrocyte sedimentation rate, C-reactive protein) have high sensitivity for GCA, but there are no specific serologic tests. The diagnosis is confirmed by temporal artery biopsy.

GCA can cause severe **ischemic optic neuropathy** due to ophthalmic artery occlusion, which can lead to blindness if not treated promptly. Other optic complications of GCA include amaurosis fugax, central or branch retinal artery occlusion, and cerebral infarction leading to central visual field defects. GCA is therefore considered a medical emergency, and physicians should not wait for biopsy before starting **glucocorticoid therapy** (eg, prednisone, methylprednisolone).

(Choice A) Acute angle-closure glaucoma causes vision loss associated with ocular pain, headache, and nausea. Examination findings include conjunctival erythema, corneal opacity, and a fixed, mid-dilated pupil. Risk factors include farsightedness (ie, hyperopia), anticholinergic drugs, and adrenergic agonists.

(Choice C) Proliferative retinopathy (ie, neovascularization of the retina) is most commonly due to longstanding, uncontrolled diabetes. Although treatment of GCA with systemic glucocorticoids can raise blood glucose, untreated GCA does not cause proliferative retinopathy.

(Choice D) Retinal detachment presents with floaters, flashing lights (photopsia), and progressive monocular vision loss. Risk factors for retinal detachment include prior eye trauma or surgery.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

blood glucose, untreated GCA does not cause proliferative retinopathy.

(Choice D) Retinal detachment presents with floaters, flashing lights (photopsia), and progressive monocular vision loss. Risk factors for retinal detachment include prior eye trauma or surgery, nearsightedness (ie, myopia), age-related macular degeneration, and diabetic retinopathy.

(Choice E) Retinal vein occlusion (RVO) presents with painless blurring of vision in a limited visual field (branch RVO) or entire eye (central RVO). Major risk factors include diabetes, hypertension, atherosclerotic disease, glaucoma, smoking, and obesity.

(Choice F) Vitreous hemorrhage causes variable-severity monocular vision loss; examination shows loss of the red reflex and obscuration of the retina. Major causes include ocular injury, anticoagulation, diabetic retinopathy, and intraocular tumors.

Educational objective:

Giant cell arteritis (GCA) is characterized by granulomatous inflammation of the media with fragmentation of the internal elastic lamina most often affecting the medium and small branches of the carotid artery. Ischemic optic neuropathy with irreversible blindness is a potential complication of GCA; therefore, patients with suspected GCA require immediate glucocorticoid therapy.

References





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 38-year-old man is evaluated due to a 2-year history of gradually worsening low back pain, bilateral buttock pain, and stiffness. Symptoms are worse in the morning and relieved with stretching and hot showers. The patient also has fatigue but no fever, chills, night sweats, or weight loss. Vital signs are normal. The patient appears healthy but has a stooped walking posture. Deep palpation over the lumbar spine at the midline and both sacroiliac joints elicits tenderness. Erythrocyte sedimentation rate is 75 mm/hr. Which of the following pathologic findings is most likely causing this patient's symptoms?

- ☐ A.Areas of bony erosions and new bone formation
- ☐ B.Areas of spindle cells and dysplastic bone
- ☐ C.Areas of trabecular and cortical bone thickening
- ☐ D.Disc protrusion and thickening of the ligamentum flava
- ☐ E.Plasma cell infiltrate in bone marrow

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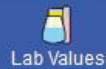
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A 38-year-old man is evaluated due to a 2-year history of gradually worsening **low back pain**, bilateral **buttock pain**, and **stiffness**. Symptoms are worse in the morning and relieved with stretching and hot showers. The patient also has fatigue but no fever, chills, night sweats, or weight loss. Vital signs are normal. The patient appears healthy but has a stooped walking posture. Deep palpation over the lumbar spine at the midline and both sacroiliac joints elicits tenderness. Erythrocyte sedimentation rate is 75 mm/hr. Which of the following pathologic findings is most likely causing this patient's symptoms?

- ✓ ☒ A. Areas of bony erosions and new bone formation (36%)
- ☐ B. Areas of spindle cells and dysplastic bone (11%)
- ☐ C. Areas of trabecular and cortical bone thickening (22%)
- ☐ D. Disc protrusion and thickening of the ligamentum flava (21%)
- ☐ E. Plasma cell infiltrate in bone marrow (7%)

Correct

 36%
Answered correctly 01 min, 21 secs
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Ankylosing spondylitis

Inflammatory back pain

- Chronic, insidious back & buttock pain
- Onset at age <40
- Worse with rest (overnight & in the morning)
- Relieved with activity & warm showers

Examination findings

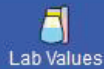
- Decreased spinal range of motion & chest expansion
- Stiff or stooped posture
- Tenderness at spine, sacroiliac joints & peripheral tendon insertions (eg, Achilles)
- Dactylitis (swelling of fingers & toes)
- Uveitis

Pathophysiology

- Increased osteoclast activity & bony erosions
- Increased bone/syndesmophyte formation

Laboratory

- Elevated ESR & CRP
- HLA-B27



anigen B27.

This patient presenting with **chronic back and buttock pain** associated with **stiffness** has **ankylosing spondylitis** (AS). The symptoms are characteristically worse in the morning and improve with stretching and warm showers. AS is most common in men age <40, and inflammatory markers (eg, erythrocyte sedimentation rate [ESR]) are usually elevated.

AS is characterized by simultaneous erosion of bone and new bone formation, unlike rheumatoid arthritis in which only erosions are seen. The initial pathogenesis is driven in part by inflammatory cytokines (eg, tumor necrosis factor, IL-17), which cause **activation of osteoclast precursor cells** and **bony erosions**. This occurs primarily in the vertebral bodies and results in destruction of the microarchitecture, increasing the risk for secondary osteoporosis and compression fractures.

Once the inflammation subsides, the reparative process leads to **excessive new bone formation** (especially in areas where fat metaplasia fills previously eroded sites); in contrast to erosion, bone formation occurs primarily at the periosteum-cartilage junction and manifests as **bridging syndesmophytes** in the vertebral column. This leads to spinal rigidity, postural alterations, and increased risk of fracture.

(Choice B) Fibrous dysplasia is a benign bone tumor characterized by focal bone dysplasia with spindle cells. It typically presents as asymptomatic lytic lesions, most commonly in the femur and tibia. Fibrous



anugen B27.

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Ankylosing spondylitis (bamboo spine)



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(Choice B) Fibrous dysplasia is a benign bone tumor characterized by focal bone dysplasia with spindle cells. It typically presents as asymptomatic lytic lesions, most commonly in the femur and tibia. Fibrous dysplasia is usually seen in children and is not an inflammatory condition (ie, normal ESR).

(Choice C) Paget disease of bone is characterized by excessive and disordered bone formation, with focal thickening of trabecular and cortical bone. Features include bone pain, fractures, and arthritis of adjacent joints. However, it is uncommon at age <50, and this patient's inflammatory back pain is more consistent with AS.

(Choice D) Intervertebral disc protrusion and thickening of the ligamentum flava can lead to spinal stenosis. The pain in this disorder typically radiates to the posterior thighs and legs and is relieved by sitting and flexion of the spine, not activity. Spinal stenosis is usually seen at age >60 and ESR is normal.

(Choice E) Multiple myeloma is characterized by plasmacytic infiltrates in the bone marrow. Patients often have back pain at night and during rest, but stiffness is less prominent. Multiple myeloma is uncommon before age 50.

Educational objective:

Ankylosing spondylitis is an inflammatory spondyloarthropathy characterized by simultaneous erosion of



(Choice C) Paget disease of bone is characterized by excessive and disordered bone formation, with focal thickening of trabecular and cortical bone. Features include bone pain, fractures, and arthritis of adjacent joints. However, it is uncommon at age <50, and this patient's inflammatory back pain is more consistent with AS.

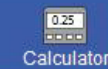
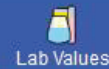
(Choice D) Intervertebral disc protrusion and thickening of the ligamentum flava can lead to spinal stenosis. The pain in this disorder typically radiates to the posterior thighs and legs and is relieved by sitting and flexion of the spine, not activity. Spinal stenosis is usually seen at age >60 and ESR is normal.

(Choice E) Multiple myeloma is characterized by plasmacytic infiltrates in the bone marrow. Patients often have back pain at night and during rest, but stiffness is less prominent. Multiple myeloma is uncommon before age 50.

Educational objective:

Ankylosing spondylitis is an inflammatory spondyloarthropathy characterized by simultaneous erosion of bone and new bone formation. Bone erosions occur primarily in vertebral bodies; however, new bone formation typically occurs at the junction of the periosteal margin and adjacent cartilage, leading to bridging syndesmophytes and ankylosis. This causes spinal rigidity, postural alterations, and increased risk of fracture.





A 12-year-old girl is brought to the emergency department following a sports injury involving the right lower extremity. The patient was playing soccer when she jumped and turned to the right to avoid being kicked by another player. She landed on her right foot with her foot internally rotated and her knee extended. Since the injury, the patient has been able to bear weight but says the knee feels unstable and she is afraid that it may give way, causing her to fall. Physical examination shows swelling of the right knee. Stability testing shows excessive anterior translation of the tibia relative to the femur. Which of the following ligaments is most likely injured?

- ☐ A. Anterior cruciate
- ☐ B. Fibular (lateral) collateral
- ☐ C. Oblique popliteal
- ☐ D. Patellar
- ☐ E. Posterior cruciate
- ☐ F. Tibial (medial) collateral





extremity. The patient was playing soccer when she jumped and turned to the right to avoid being kicked by another player. She landed on her right foot with her foot **internally rotated** and her knee **extended**. Since the injury, the patient has been able to bear weight but says the knee feels unstable and she is afraid that it may give way, causing her to fall. Physical examination shows swelling of the right knee. Stability testing shows **excessive anterior translation** of the tibia relative to the femur. Which of the following ligaments is most likely injured?

- ✓ ☒ A. Anterior cruciate (87%)
- ☐ B. Fibular (lateral) collateral (2%)
- ☐ C. Oblique popliteal (0%)
- ☐ D. Patellar (1%)
- ☐ E. Posterior cruciate (6%)
- ☐ F. Tibial (medial) collateral (1%)

Correct

87%

01 min, 03 secs

01/08/2021

Block Time Remaining: 00:36:25

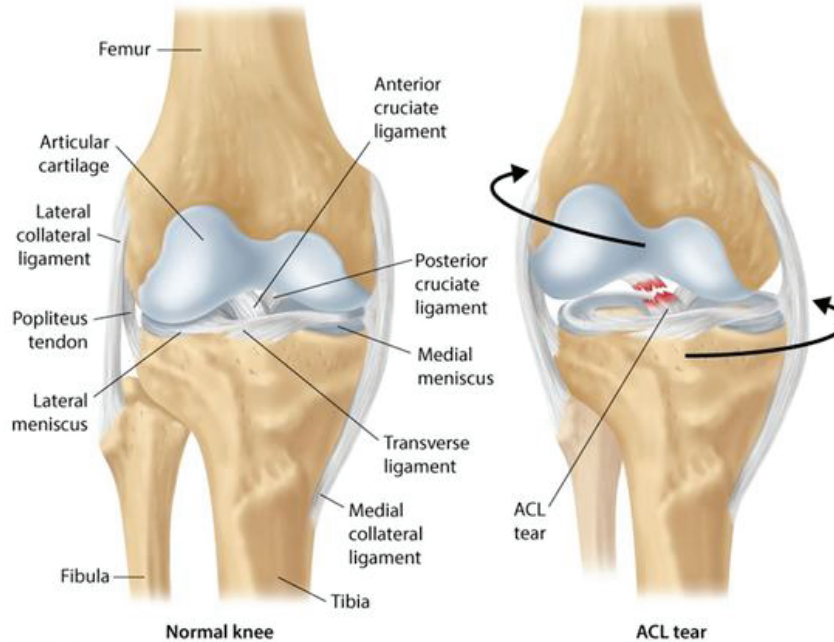
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End Block

Exhibit Display

ACL tear



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Mark

Previous

Next



Full Screen



Tutorial



Lab Values



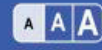
Notes



Calculator



Reverse Color



Text Zoom



Settings



The **anterior cruciate ligament** (ACL) originates on the lateral femoral condyle and courses anteriorly and medially to insert on the anterior intercondylar area of the tibia. The primary function of the ACL is to **prevent anterior motion** of the tibia with respect to the femur, although it also plays a role in stabilizing the knee against rotatory and varus/valgus forces.

The ACL is most commonly ruptured in noncontact sports that involve sudden changes in direction or excessive internal rotation or lateral (valgus) bending forces when landing from a jump. The middle geniculate artery provides the primary blood supply to the ACL, and injuries are characterized by rapid-onset **hemarthrosis** and knee swelling. In addition to the effusion, examination typically shows **anterior laxity** of the tibia relative to the femur (eg, [Lachman test](#), [anterior drawer test](#)).

(Choices B and F) The [tibial \(medial\) collateral ligament](#) is most commonly injured by impacts to the lateral knee. The fibular (lateral) collateral ligament is only rarely injured but may be injured by a forceful blow to the medial knee while the leg is extended. Injury to these ligaments is characterized by laxity of valgus or varus stress, respectively.

(Choice C) The oblique popliteal ligament is a wide, fibrous band that connects the posterior distal femur



Exhibit Display

Tests for anterior cruciate ligament tear

Anterior drawer test



Lachman test



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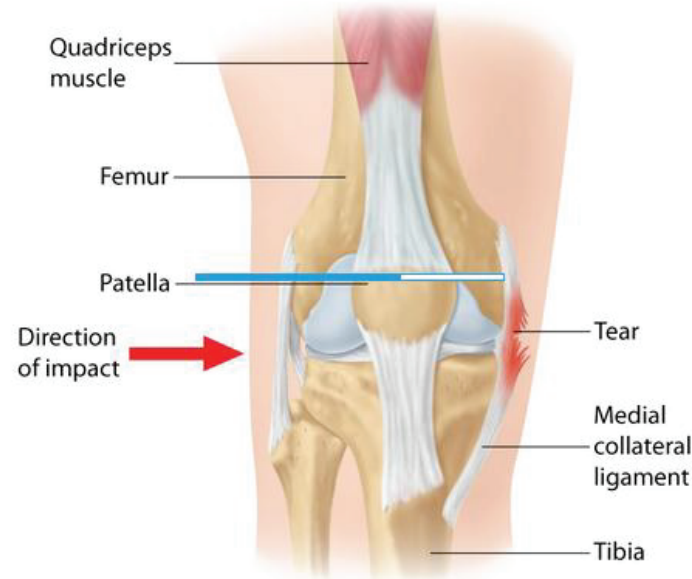
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Exhibit Display

Medial collateral ligament injury



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New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice C) The oblique popliteal ligament is a wide, fibrous band that connects the posterior distal femur to the posterior proximal tibia. It has small openings for nerves, vessels, and muscle insertions. Injury would allow laxity of knee hyperextension.

(Choice D) The patellar ligament (tendon) is a very robust structure that represents the inferior projection of the quadriceps femoris tendon. Injury causes impaired knee extension.

(Choice E) The **posterior cruciate ligament** extends from the medial condyle of the femur to the posterior head of the tibia. Injury causes laxity of posterior movement of the tibia with respect to the femur (eg, posterior drawer test).

Educational objective:

The anterior cruciate ligament (ACL) can be damaged by sudden changes in direction or awkward landings (eg, excessive internal rotation or valgus stress) during sports activity. ACL tears are typically associated with rapid-onset hemarthrosis. Physical examination shows anterior laxity of the tibia relative to the femur (eg, Lachman test, anterior drawer test).

Anatomy

Rheumatology/Orthopedics & Sports

Knee trauma

Subject

System

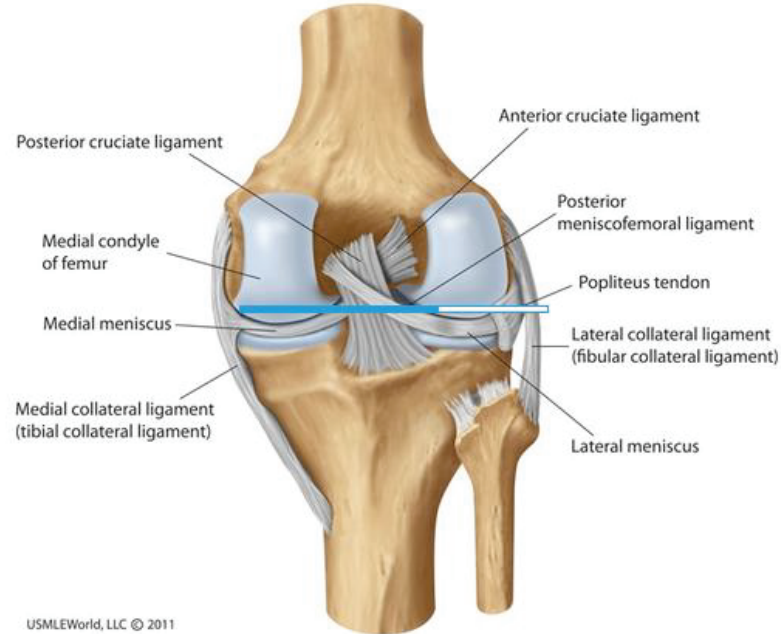
Topic



(Choice C) The oblique popliteal ligament is a wide fibrous band that connects the posterior distal femur

Exhibit Display

Knee: posterior view



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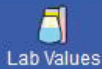
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Zoom Out

Reset

New | Existing

My Notebook



A 35-year-old man with a known history of peptic ulcer disease comes to the physician with sudden onset of pain, swelling, and redness at the base of his great toe. The patient was awakened in the middle of the night by the pain and was unable to go back to sleep. He has no history of trauma to the joint. Physical examination shows swelling, erythema, and exquisite tenderness involving the right first metatarsophalangeal joint. Fine-needle aspiration of the joint shows needle-shaped, negatively birefringent crystals. After making the diagnosis, the physician prescribes an appropriate medication. Shortly after starting the medication, the patient develops nausea, vomiting, and diarrhea. Which of the following is the most likely mechanism of action of the drug prescribed to this patient?

- ☐ A. Decreased renal tubular uric acid reabsorption
- ☐ B. Inhibition of cyclooxygenase activity
- ☐ C. Inhibition of microtubule formation
- ☐ D. Inhibition of phospholipase A₂ activity
- ☐ E. Inhibition of xanthine oxidase activity



of pain, swelling, and redness at the base of his great toe. The patient was awakened in the middle of the night by the pain and was unable to go back to sleep. He has no history of trauma to the joint. Physical examination shows swelling, erythema, and exquisite tenderness involving the right first metatarsophalangeal joint. Fine-needle aspiration of the joint shows needle-shaped, negatively birefringent crystals. After making the diagnosis, the physician prescribes an appropriate medication. Shortly after starting the medication, the patient develops nausea, vomiting, and diarrhea. Which of the following is the most likely mechanism of action of the drug prescribed to this patient?

- ☐ A. Decreased renal tubular uric acid reabsorption (3%)
- ☐ B. Inhibition of cyclooxygenase activity (12%)
- ☒ C. Inhibition of microtubule formation (64%)
- ☐ D. Inhibition of phospholipase A₂ activity (1%)
- ☐ E. Inhibition of xanthine oxidase activity (17%)

Correct

64%
Answered correctly50 secs
Time Spent11/06/2020
Last Updated



Acute gouty arthritis

| | |
|-----------------------------|--|
| Signs & symptoms | <ul style="list-style-type: none">• Usually involves first metatarsophalangeal joint or knee• Swelling, erythema & exquisite tenderness• Symptoms develop rapidly over 24 hr |
| Diagnosis | <ul style="list-style-type: none">• Joint aspiration shows needle-shaped, negatively birefringent crystals |
| Treatment | <ul style="list-style-type: none">• Nonsteroidal anti-inflammatory drugs (eg, naproxen, indomethacin) preferred if no contraindications• Colchicine used as second-line therapy |

Acute onset of pain and swelling of the first metatarsophalangeal joint and joint aspiration showing needle-shaped, negatively birefringent crystals are diagnostic for acute gouty arthritis. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the mainstay of treatment for most patients. However, colchicine is often used in patients with mild-to-moderate renal failure, peptic ulcer disease, or other contraindications to NSAIDs. Colchicine is an effective anti-inflammatory agent in acute gouty arthritis and acts by binding to the intracellular protein tubulin, preventing tubulin polymerization into microtubules. This leads to impaired leukocyte migration and phagocytosis, reducing the inflammation seen in gouty arthritis. Because





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

NSAIDs. Colchicine is an effective anti-inflammatory agent in acute gouty arthritis and acts by binding to the intracellular protein tubulin, preventing tubulin polymerization into microtubules. This leads to impaired leukocyte migration and phagocytosis, reducing the inflammation seen in gouty arthritis. Because colchicine also disrupts microtubule formation in gastrointestinal mucosal cells, many patients develop diarrhea and, less commonly, nausea, vomiting, and abdominal pain.

(Choices A and E) Probenecid decreases proximal tubular uric acid reabsorption, and allopurinol inhibits xanthine oxidase (converts xanthine to uric acid). These medications are prescribed to lower serum uric acid levels in chronic gout. These agents are contraindicated in acute gouty arthritis as they can mobilize tissue stores of uric acid and precipitate or worsen acute attacks.

(Choice B) NSAIDs induce their anti-inflammatory effects by inhibiting cyclooxygenase (COX)-1 and COX-2 isoenzymes, thus blocking prostaglandin synthesis. Because they can cause significant gastrointestinal irritation (eg, nausea, dyspepsia, bleeding), their use is contraindicated in patients with peptic ulcer disease.

(Choice D) Glucocorticosteroids exert their anti-inflammatory effect by inhibiting phospholipase A₂ activity. These medications can be used in acute gout and are not associated with significant diarrhea.

Educational objective:





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

xanthine oxidase (converts xanthine to uric acid). These medications are prescribed to lower serum uric acid levels in chronic gout. These agents are contraindicated in acute gouty arthritis as they can mobilize tissue stores of uric acid and precipitate or worsen acute attacks.

(Choice B) NSAIDs induce their anti-inflammatory effects by inhibiting cyclooxygenase (COX)-1 and COX-2 isoenzymes, thus blocking prostaglandin synthesis. Because they can cause significant gastrointestinal irritation (eg, nausea, dyspepsia, bleeding), their use is contraindicated in patients with peptic ulcer disease.

(Choice D) Glucocorticosteroids exert their anti-inflammatory effect by inhibiting phospholipase A₂ activity. These medications can be used in acute gout and are not associated with significant diarrhea.

Educational objective:

Colchicine is a second-line agent for treating acute gouty arthritis. It inhibits tubulin polymerization and microtubule formation in leukocytes, reducing neutrophil chemotaxis and emigration to sites inflamed by tissue deposition of monosodium urate crystals. Gastrointestinal mucosal function is also impaired by microtubule disruption, leading to diarrhea and, less commonly, nausea, vomiting, and abdominal pain.

References

- [Safety profile of anti-gout agents: an update.](#)



1



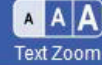
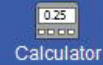
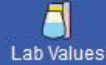
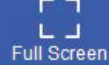
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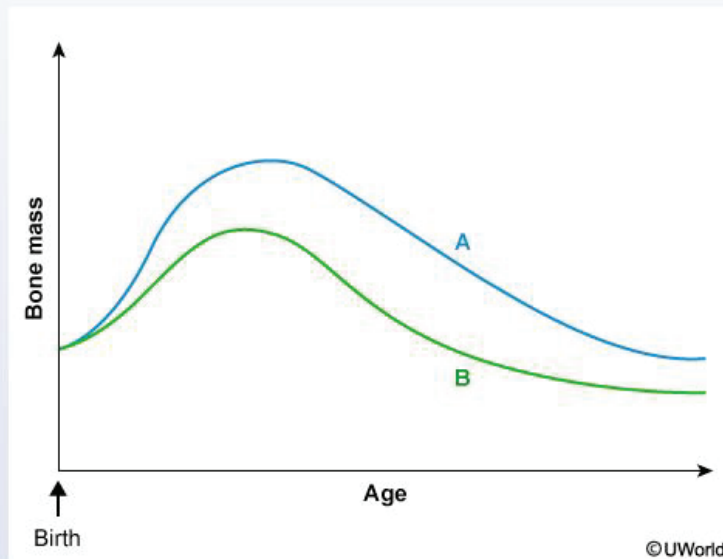
Suspend



End Block



A prospective observational study is performed to determine factors affecting bone mass and fracture risk. Detailed demographic and clinical information is obtained from a large number of volunteers, and bone mass is monitored over time. The data obtained from 2 specific groups of women are shown below.



Which of the following factors is most likely present in group A?





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

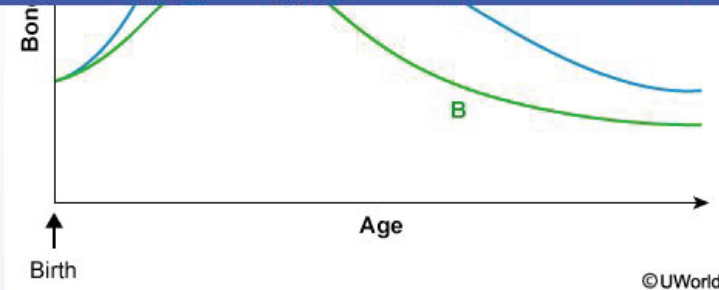
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following factors is most likely present in group A?

- ☐ A. Early menopause
- ☐ B. Increased physical activity
- ☐ C. Lower body mass index
- ☐ D. Positive smoking history
- ☐ E. Use of glucocorticoids

Submit



Previous

Next

Full Screen

Tutorial

Lab Values

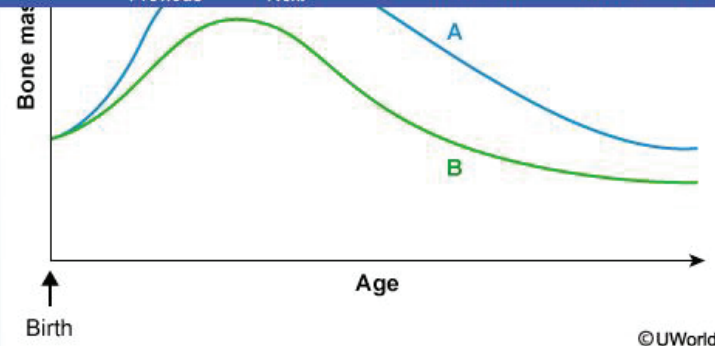
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following factors is most likely present in group A?

- ☐ A. ~~Early menopause~~ (1%)
- ☒ B. Increased physical activity (94%)
- ☐ C. ~~Lower body mass index~~ (2%)
- ☐ D. ~~Positive smoking history~~ (0%)
- ☐ E. Use of glucocorticoids (0%)





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Risk factors for osteoporotic fractures

| Nonmodifiable | Potentially modifiable |
|---|---|
| <ul style="list-style-type: none">• Advancing age• Female sex• White, Hispanic, or Asian ethnicity• Personal or family history of fracture | <ul style="list-style-type: none">• Decreased physical activity• Low body weight• Poor calcium & vitamin D intake• Excessive alcohol or tobacco use• Premature menopause• Glucocorticoid use |

Bone mass in adulthood is determined by **peak bone mass** and the subsequent rate of **bone loss**. Most of the variation in peak bone mass is genetically determined, but environmental factors such as nutritional status (eg, calcium and vitamin D intake) and physical activity also have a significant impact.

Establishment of a high peak bone mass during early adulthood is important because bone mass subsequently declines with age. By convention, **osteoporosis** is defined as a bone density that is 2.5 or more standard deviations below the mean (T score ≤ -2.5) for peak young adult bone density.

The subjects in group A show a higher peak bone mass, slightly lower rate of post-peak bone loss, and higher late-life bone mass than the subjects in group B. This is consistent with the effects of regular





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

more standard deviations below the mean (T score ≤ -2.5) for peak young adult bone density.

The subjects in group A show a higher peak bone mass, slightly lower rate of post-peak bone loss, and higher late-life bone mass than the subjects in group B. This is consistent with the effects of regular **exercise**, especially weight-bearing exercise. In contrast, factors that lead to a lower peak bone mass include genetic and ethnic factors (eg, Asian or Caucasian ethnicity), chronic inflammatory disease, exposure to glucocorticoid medications, and sedentary lifestyle. In addition, prolonged caloric deficits (often seen with excessive exercise) can lead to functional hypothalamic amenorrhea, suppression of estrogen production, and rapid bone loss.

(Choice A) Estrogens have an anabolic effect on bone by increasing osteoblastic activity and decreasing osteoclastic activity. Loss of estrogen effect (eg, menopause, premature ovarian failure) causes accelerated bone loss.

(Choice C) Bone density is proportional to BMI. BMI $<22 \text{ kg/m}^2$ (or weight $<57.6 \text{ kg}$ [127 lb]) is associated with increased risk for osteoporosis.

(Choice D) Smoking causes accelerated bone loss and is a major risk factor for osteoporosis and osteoporotic fractures.

(Choice E) Chronic glucocorticoid use is a major risk factor for osteoporosis. Glucocorticoids decrease





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

accelerated bone loss.

(Choice C) Bone density is proportional to BMI. BMI $<22 \text{ kg/m}^2$ (or weight $<57.6 \text{ kg}$ [127 lb]) is associated with increased risk for osteoporosis.

(Choice D) Smoking causes accelerated bone loss and is a major risk factor for osteoporosis and osteoporotic fractures.

(Choice E) Chronic glucocorticoid use is a major risk factor for osteoporosis. Glucocorticoids decrease the gastrointestinal absorption of calcium, inhibit collagen synthesis by osteoblasts, decrease GnRH (leading to hypogonadism), and increase urinary calcium loss.

Educational objective:

Regular exercise leads to increased peak bone mass, a reduced rate of bone loss, and a decreased risk of osteoporosis.

References

- [Exercise for preventing and treating osteoporosis in postmenopausal women.](#)

Physiology

Rheumatology/Orthopedics & Sports

Osteoporosis

Subject

System

Topic

Block Time Remaining: 00:38:16

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1



Feedback



Suspend



End Block

A 29-year-old woman is evaluated for severe left hip pain after twisting her leg. She has bony deformities of the lower extremities, and her mobility is limited. The patient has a history of hyperthyroidism, which was managed with radioiodine therapy. Menarche was at age 7, and she has regular 30-day cycles. Physical examination shows large, hyperpigmented macules with irregular borders located on the left shoulder, left side of the neck, and left buttock. X-ray findings are shown in the image below.

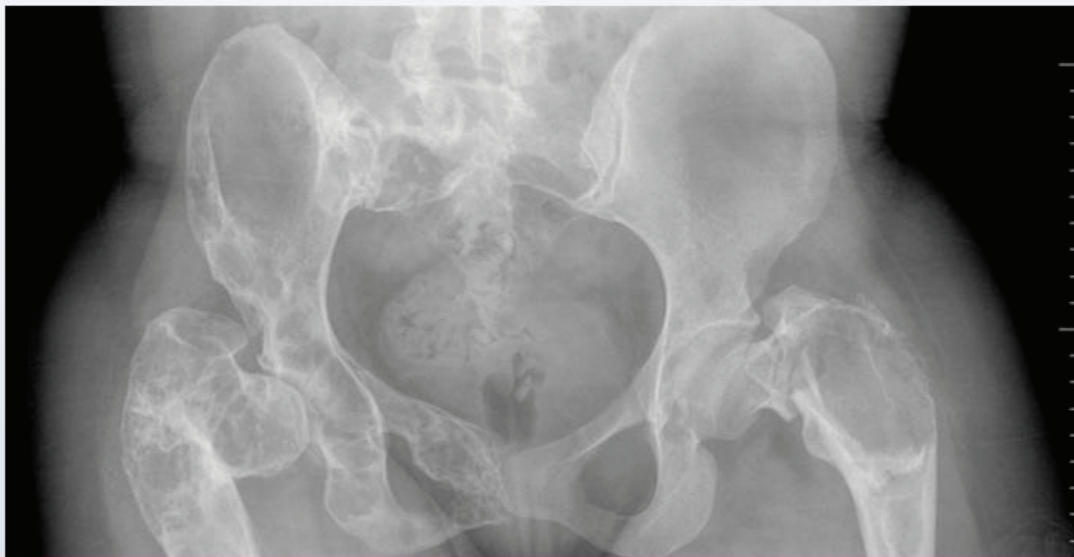
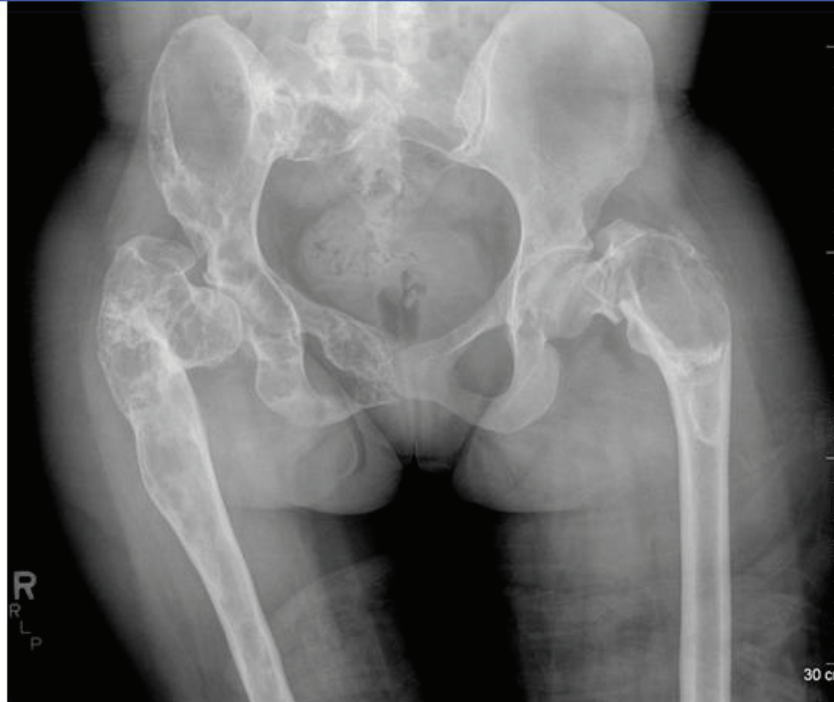


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Mark



Previous



Next



Full Screen



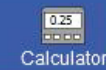
Tutorial



Lab Values



Notes



Calculator



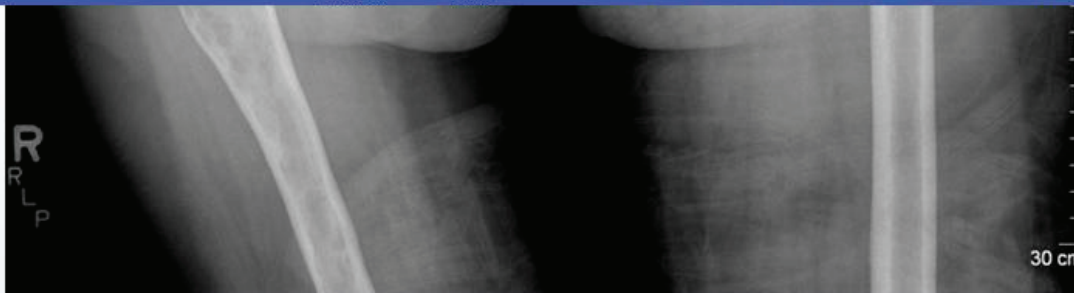
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Text Zoom



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Which of the following is the most likely diagnosis?

- ☐ A. Ewing sarcoma
- ☐ B. Gaucher disease
- ☐ C. Legg-Calvé-Perthes disease
- ☐ D. McCune-Albright syndrome
- ☐ E. Neurofibromatosis type 1

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2



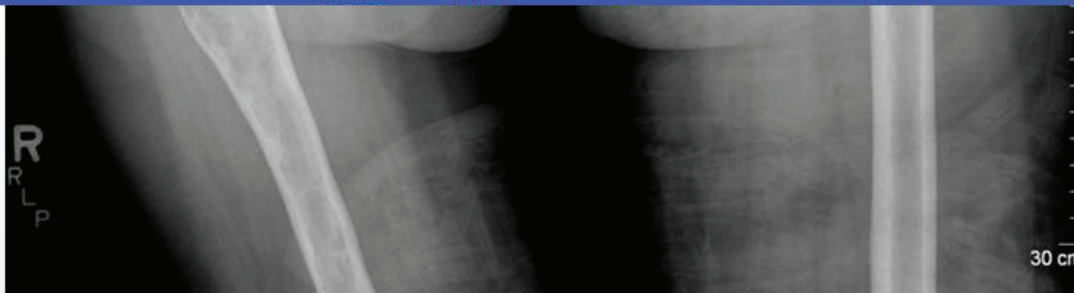
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Suspend



End Block



Which of the following is the most likely diagnosis?

- ☐ A. Ewing sarcoma (7%)
- ☐ B. Gaucher disease (5%)
- ☐ C. Legg-Calvé-Perthes disease (14%)
- ☒ D. McCune-Albright syndrome (54%)
- ☐ E. Neurofibromatosis type 1 (18%)

Correct

54%



01 min, 49 secs



03/14/2021

Block Time Remaining: 00:40:05

TUTOR

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Feedback

Suspend

End Block

McCune-Albright syndrome

Pathogenesis

- Mutation *GNAS* gene
- Constant G protein activation
- Hormone overproduction

Clinical features

- Peripheral precocious puberty
- Irregular café-au-lait macules
- Polyostotic fibrous dysplasia

Complications

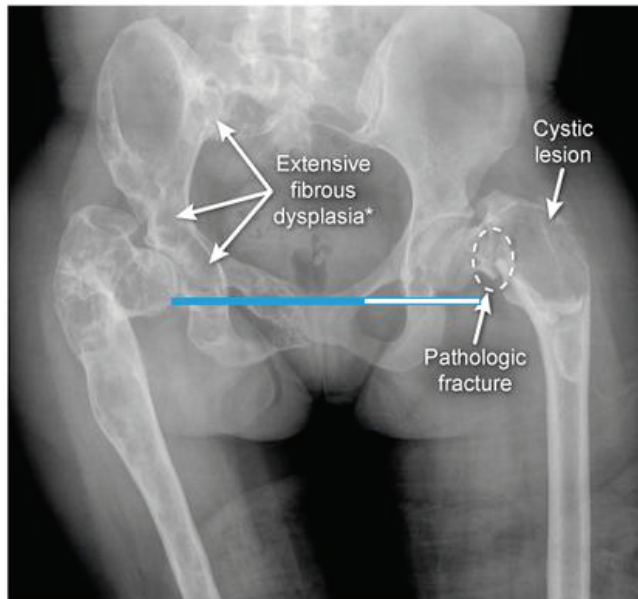
- Thyrotoxicosis
- Acromegaly
- Cushing syndrome

This patient's **triad** of fibrous dysplasia (multiple osteolytic-appearing lesions of the hip and pelvis), endocrine abnormalities, and café-au-lait spots suggests a diagnosis of McCune-Albright syndrome (MAS). Her **x-ray** reveals a pathological fracture through the left hip in the region of fibrous dysplasia.

MAS results from a mosaic somatic mutation during embryogenesis in the *GNAS* gene encoding the stimulatory α -subunit of G protein. This mutation causes constitutive activation of the G protein/cAMP

Exhibit Display

McCune-Albright syndrome



*Replacement of normal bone with fibrous tissue and immature bone

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Zoom Out

Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(MAS). Her **x-ray** reveals a pathological fracture through the left hip in the region of fibrous dysplasia.

MAS results from a mosaic somatic mutation during embryogenesis in the *GNAS* gene encoding the stimulatory α subunit of G protein. This mutation causes constitutive activation of the G protein/cAMP/adenylate cyclase signaling cascade, which leads to a gain of function of the affected cells. Persistent G-protein stimulatory activity in melanocytes results in prominent **café-au-lait macules (CALMs)**. CALMs, usually the first manifestation of MAS, are often large and unilateral with an irregular, "coast of Maine" border.

In addition, autonomous endocrine function most commonly results in **precocious puberty** (onset of secondary sexual development before age 8 in girls). The mutation also results in increased proliferation of fibroblast-like cells, increased secretion of IL-6, and activation of osteoclasts (**fibrous dysplasia**). The term polyostotic refers to the presence of lesions in many bones, although they are typically unilateral.

(Choice A) Ewing sarcoma typically presents as a single lesion with months of pain and swelling in one of the long bones of the extremities or pelvis. Multiple layers of periosteal reaction result in a characteristic "onion peel" appearance on x-ray.

(Choice B) Gaucher disease is an inherited lysosomal storage disease that is most common among Ashkenazi Jews and may also result in diffuse, painful lytic bone lesions. However, it leads to delayed



2



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

union peel appearance on x-ray.

(Choice B) Gaucher disease is an inherited lysosomal storage disease that is most common among Ashkenazi Jews and may also result in diffuse, painful lytic bone lesions. However, it leads to delayed puberty and growth.

(Choice C) [Legg-Calvé-Perthes disease](#) is a disease of young children that results in isolated idiopathic osteonecrosis of the hip (red circle).

(Choice E) Neurofibromatosis type 1 (NF1) is characterized by [CALMs](#) that are usually smaller, bilateral, and have a relatively smooth border ("coast of California"). These CALMs are usually accompanied by axillary/inguinal freckling and cutaneous [neurofibromas](#). Bony abnormalities of NF1 include long-bone dysplasia (tibial bowing) and pseudoarthrosis that typically present in toddlers.

Educational objective:

McCune-Albright syndrome is characterized by the triad of fibrous dysplasia of the bone, endocrine abnormalities, and café-au-lait spots. The condition results from an activating mutation in the G protein/CAMP/adenylate cyclase signaling pathway.

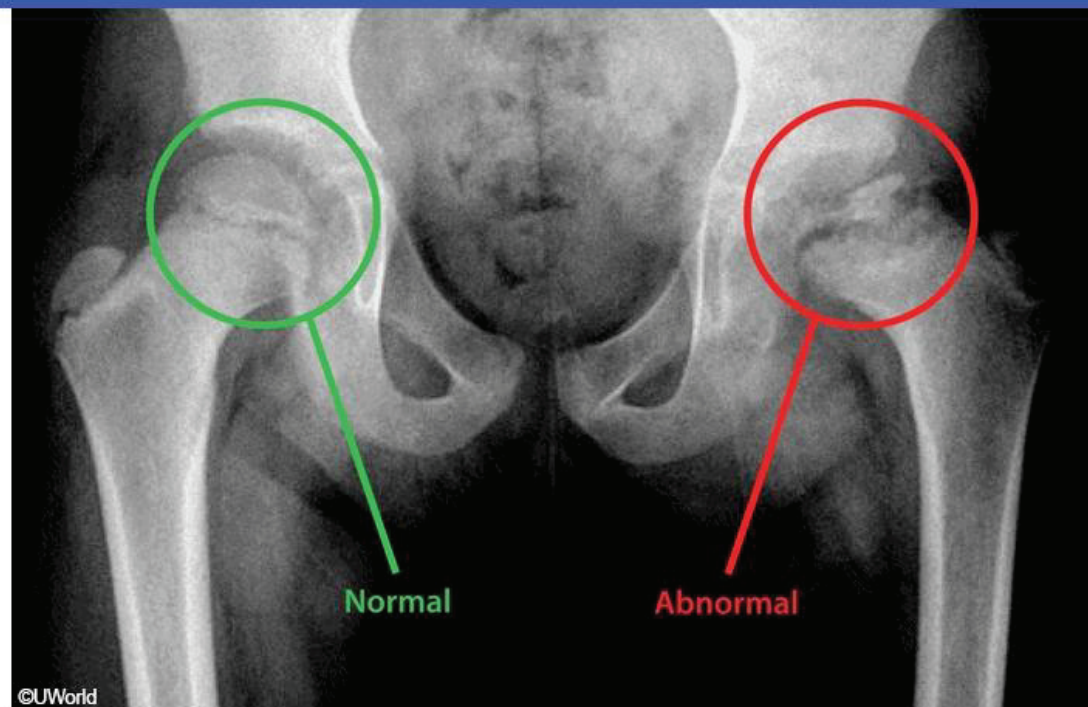
References

- [McCune-Albright syndrome](#).



onion peel appearance on x-ray.

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Zoom Out

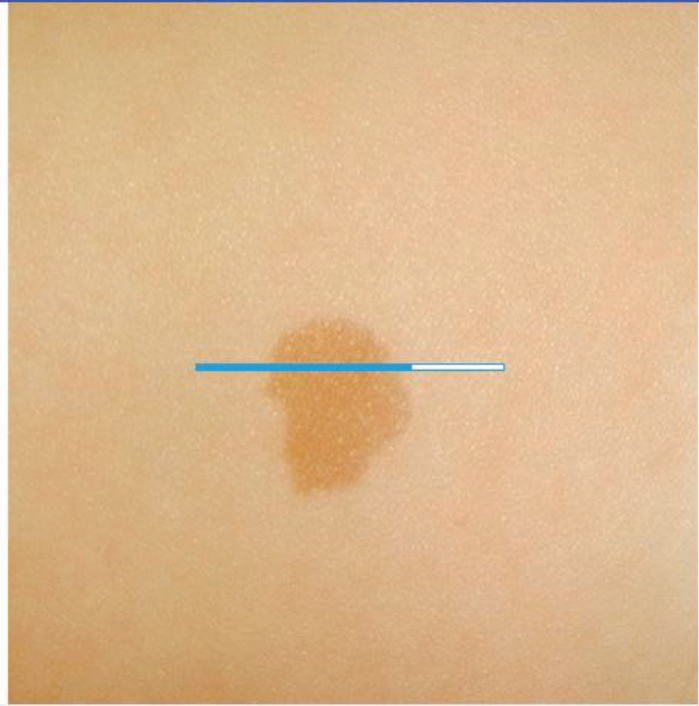
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New | Existing

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onion peel appearance on x-ray.

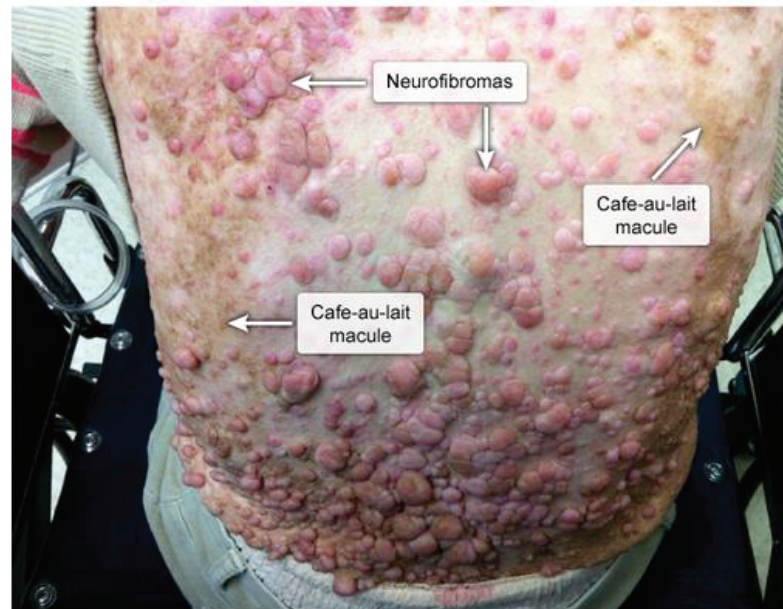
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onion peel appearance on x-ray.

Exhibit Display

Neurofibromatosis type 1



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Zoom Out

Reset

New | Existing

My Notebook



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 26-year-old man comes to the emergency department due to fever, right flank pain, and difficulty walking for the past 3 days. A week ago, the patient was treated with cephalexin for bacterial folliculitis. He was diagnosed with type I diabetes mellitus 10 years ago and takes subcutaneous insulin. Temperature is 38.9° C (102° F). During the medical interview, the patient lies supine on the examination table with his right hip and knee flexed and the limb externally rotated. On physical examination, he resists passive extension of the limb due to worsening of the pain. This patient's pathological process most likely involves which of the following muscles?

- ☐ A. Obturator externus
- ☐ B. Psoas major
- ☐ C. Quadratus lumborum
- ☐ D. Rectus femoris
- ☐ E. Transversus abdominis

Submit

Block Time Remaining: 00:40:06

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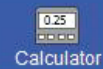
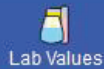
Feedback



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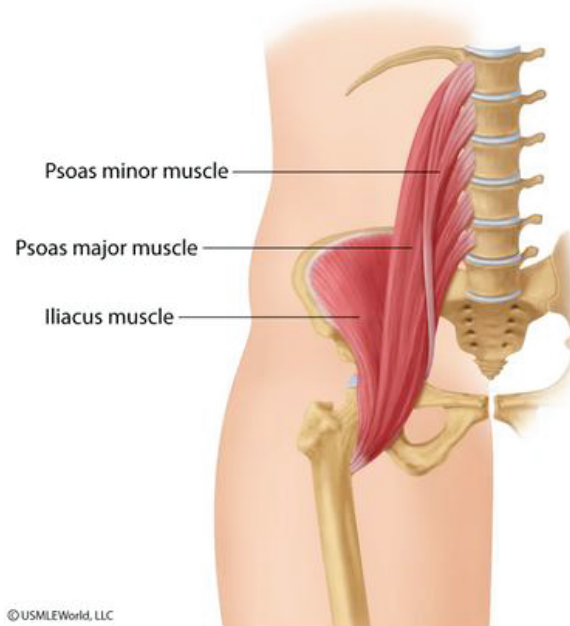
A 26-year-old man comes to the emergency department due to fever, right flank pain, and difficulty walking for the past 3 days. A week ago, the patient was treated with cephalexin for bacterial folliculitis. He was diagnosed with type I diabetes mellitus 10 years ago and takes subcutaneous insulin. Temperature is 38.9° C (102° F). During the medical interview, the patient lies supine on the examination table with his right hip and knee flexed and the limb externally rotated. On physical examination, he resists passive extension of the limb due to worsening of the pain. This patient's pathological process most likely involves which of the following muscles?

- ☐ A. Obturator externus (9%)
- ☒ B. Psoas major (68%)
- ☐ C. Quadratus lumborum (8%)
- ☐ D. Rectus femoris (12%)
- ☐ E. Transversus abdominis (1%)



Exhibit Display

The iliopsoas muscle



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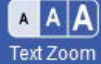
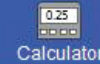
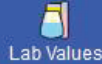
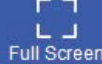
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This patient most likely has a **psoas abscess**. The psoas muscle arises from the transverse processes and lateral aspects of the 12th thoracic through 5th lumbar vertebrae. It then courses downward across the pelvic brim anterior to the hip joint capsule and deep to the inguinal ligament to insert into the lesser trochanter of the femur via a tendon shared with the iliacus muscle. The iliacus and psoas muscles act as the major hip flexors.

Psoas abscesses can occur due to direct spread of infection from an adjacent structure (eg, vertebral bodies, appendix, hip joint) or from **hematogenous** or lymphatic **seeding** from a distant and sometimes unknown site (in this case, the patient's skin infection). Risk factors include diabetes mellitus, intravenous drug use, HIV infection, and other forms of immunosuppression.

Signs and symptoms of a psoas abscess include **fever**, back or **flank pain**, inguinal mass, and difficulty walking. **Pain is exacerbated** by movements that cause the psoas muscle to be stretched or extended (which causes irritation of the muscle fibers), such as **extension at the hip** (ie, psoas sign). As such, patients frequently position themselves to reduce discomfort by minimizing psoas stretching, particularly with hip flexion, external rotation, and lumbar lordosis.

The psoas sign can also occur in acute appendicitis when the appendix is retrocecal (ie, located behind the cecum), as the inflamed appendix lies upon the right psoas muscle, causing irritation.



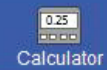
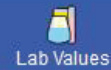


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cecum) as the inflamed appendix lies upon the right psoas muscle, causing irritation

Block Time Remaining: 00:41:32

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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with hip flexion, external rotation, and lumbar lordosis.

The psoas sign can also occur in acute appendicitis when the appendix is retrocecal (ie, located behind the cecum), as the inflamed appendix lies upon the right psoas muscle, causing irritation.

(Choice A) The obturator externus runs from the obturator foramen of the pelvis to the trochanteric fossa of the femur. It acts to externally rotate the thigh.

(Choice C) The **quadratus lumborum** courses posterior to the psoas muscle. It connects the 12th rib and upper lumbar vertebra to the iliac crest. Contraction of this muscle assists in extension and lateral flexion of the vertebral column.

(Choice D) The rectus femoris is 1 of 4 quadriceps muscles that attach to the patella via the shared quadriceps tendon. It functions to extend the knee and flex the thigh. A patient with an abscess involving this muscle would most likely complain of thigh or knee pain and favor extension at the knee.

(Choice E) The transversus abdominis is the deepest of the 3 anterolaterally coursing **abdominal wall muscles**. It helps maintain posture and increases intraabdominal pressure during forced expiration and defecation.

Educational objective:

Deep abscess presents with fever, back or flank pain, an inguinal mass, and difficulty walking.



1



Feedback



Suspend



End Block



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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with hip flexion, external rotation, and lumbar lordosis.

Exhibit Display

Muscles of the hip

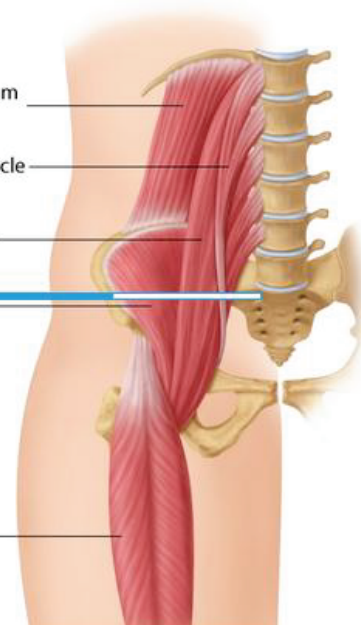
Quadratus lumborum
muscle

Psoas minor muscle

Psoas major muscle

Iliacus muscle

Rectus femoris
muscle



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1



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Suspend



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Mark

Previous

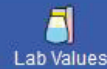
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Full Screen



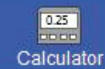
Tutorial



Lab Values



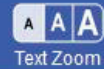
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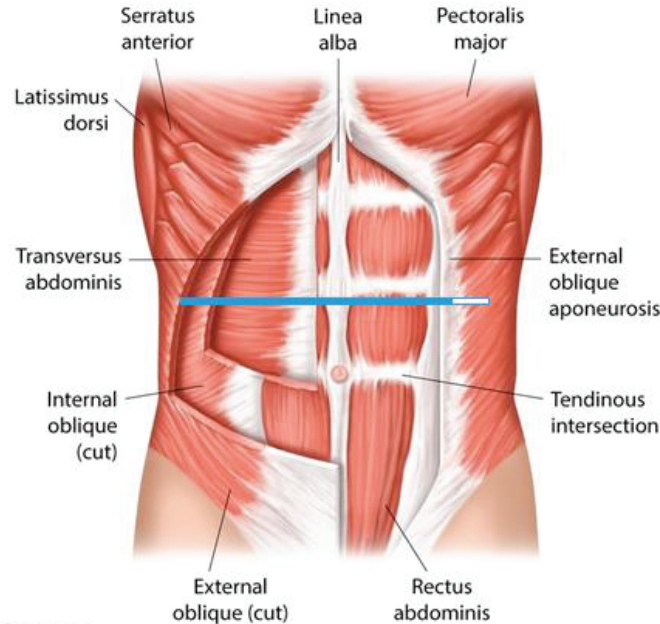


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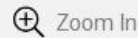
with hip flexion, external rotation, and lumbar lordosis.

Exhibit Display

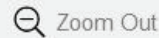
Abdominal wall musculature



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Zoom In



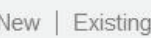
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(Choice C) The quadratus lumborum courses posterior to the psoas muscle. It connects the 12th rib and upper lumbar vertebra to the iliac crest. Contraction of this muscle assists in extension and lateral flexion of the vertebral column.

(Choice D) The rectus femoris is 1 of 4 quadriceps muscles that attach to the patella via the shared quadriceps tendon. It functions to extend the knee and flex the thigh. A patient with an abscess involving this muscle would most likely complain of thigh or knee pain and favor extension at the knee.

(Choice E) The transversus abdominis is the deepest of the 3 anterolaterally coursing abdominal wall muscles. It helps maintain posture and increases intraabdominal pressure during forced expiration and defecation.

Educational objective:

Psoas abscess presents with fever, back or flank pain, an inguinal mass, and difficulty walking.

Inflammation of the psoas muscle leads to pain with extension at the hip (ie, psoas sign). Psoas abscess can develop due to hematogenous or lymphatic seeding from a distant site, particularly in patients with diabetes mellitus, intravenous drug use, and immunosuppression (eg, HIV infection).

Anatomy

Rheumatology/Orthopedics & Sports

Psoas abscess

Subject

System

Topic





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Reverse Color



Text Zoom



Settings

A 15-year-old boy comes to the office due to right arm numbness. He plays on his high school baseball team and has been intensively practicing his pitching for an upcoming game. For the past several weeks, the patient has had fluctuating tingling and numbness involving the right shoulder, arm, and hand. He also has recently developed dull pain in the right little finger and hand. The symptoms worsen with overhead activities and when throwing a baseball. The patient has no medical problems other than being told that he has an extra rib. On examination, there is right-sided weakness of the intrinsic hand muscles. Which of the following muscles is most likely contributing to this patient's condition?

- ☐ A. Coracobrachialis muscle
- ☐ B. Scalene muscles
- ☐ C. Subscapularis muscle
- ☐ D. Teres major muscle
- ☐ E. Triceps brachii

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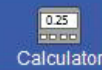
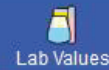
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A 15-year-old boy comes to the office due to **right arm numbness**. He plays on his high school baseball team and has been intensively practicing his pitching for an upcoming game. For the past several weeks, the patient has had **fluctuating tingling** and **numbness** involving the right shoulder, arm, and hand. He also has recently developed dull pain in the right little finger and hand. The symptoms worsen with overhead activities and when throwing a baseball. The patient has no medical problems other than being told that he has an extra rib. On examination, there is right-sided weakness of the intrinsic hand muscles. Which of the following muscles is most likely contributing to this patient's condition?

- ☐ A. Coracobrachialis muscle (11%)
- ☒ B. Scalene muscles (59%)
- ☐ C. Subscapularis muscle (17%)
- ☐ D. Teres major muscle (4%)
- ☐ E. Triceps brachii (6%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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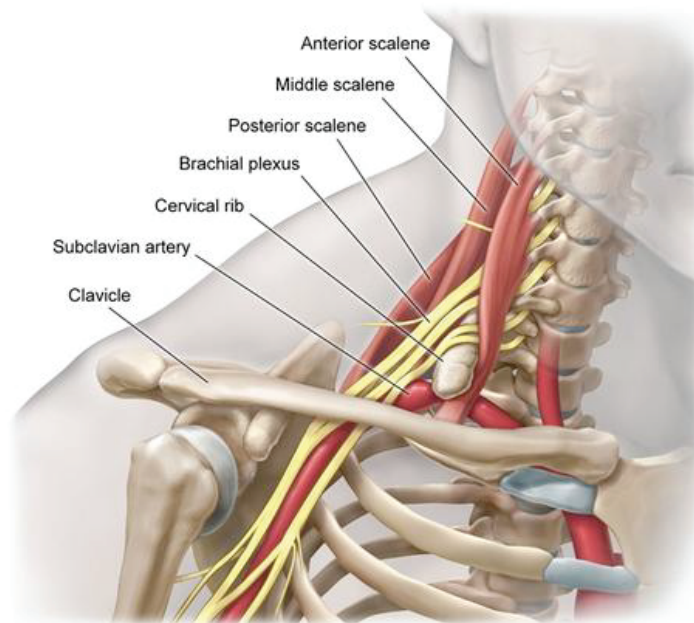
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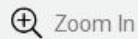
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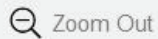
Thoracic outlet syndrome



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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This patient's upper extremity neurologic symptoms in the setting of an extra rib are highly suggestive of **thoracic outlet syndrome (TOS)**. The thoracic outlet refers to the region above the first rib and behind the clavicle that is bordered by the cervical vertebral bones and the sternum. **Compression** of the **brachial plexus** as it passes through the thoracic outlet can cause upper extremity numbness, tingling, and weakness (most often in an ulnar distribution due to compression of the lower trunk). Involvement of the **subclavian vein and artery** can also occur and lead to upper extremity swelling and exertional arm pain.

TOS most commonly occurs due to compression of the brachial plexus within the **scalene triangle**, which is formed by the anterior and middle scalene muscles and the first rib. The anterior scalene muscle originates from the C3-C6 transverse processes and attaches to the scalene tubercle of the first rib. The middle scalene originates from the C2-C7 transverse processes and inserts into the posterior portion of the first rib. The brachial plexus trunks and subclavian artery pass between the anterior and middle scalenes; the subclavian vein runs anterior to the anterior scalene.

The presence of an **anomalous cervical rib** or scalene muscular anomalies can predispose to TOS. Affected patients typically have a history of trauma or repetitive overhead arm movements (eg, swimming, stacking boxes).



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stacking boxes).

(Choice A) The **coracobrachialis** originates from the coracoid process of the scapula and acts to flex the arm at the glenohumeral joint. The musculocutaneous nerve pierces the muscle near its insertion into the humerus; overuse of the coracobrachialis (eg, excessive bench pressing) can cause entrapment of the musculocutaneous nerve, causing impaired elbow flexion and lateral forearm sensory loss.

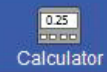
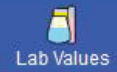
(Choice C) The **subscapularis muscle** originates in the subscapular fossa of the scapula and inserts into the lesser tubercle of the humerus. It acts to adduct and internally rotate the humerus.

(Choices D and E) The teres major muscle and long head of the triceps brachii form the inferior and medial borders of the **quadrangular space** through which the axillary nerve passes. Entrapment of the axillary nerve within the quadrangular space can cause sensory loss over the lateral shoulder and impair shoulder abduction.

Educational objective:

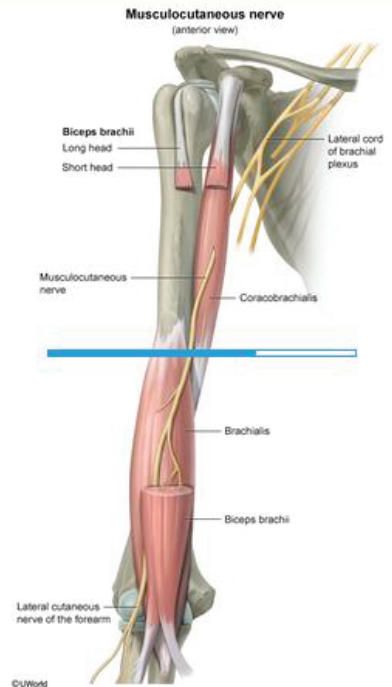
Thoracic outlet syndrome (TOS) is most often caused by compression of the brachial plexus as it passes through the scalene triangle, the space bordered by the anterior and middle scalene muscles and the first rib. Symptoms typically include upper extremity numbness, tingling, and weakness that worsen with repetitive overhead arm movements. The presence of an anomalous cervical rib is a risk factor for TOS.





stacking boxes)

Exhibit Display



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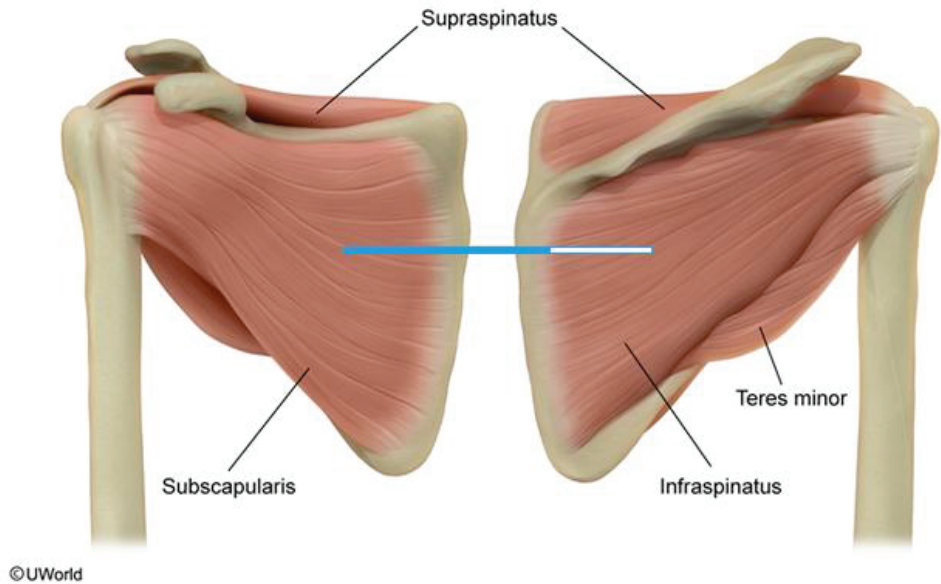
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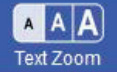
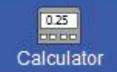
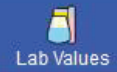
Exhibit Display

Rotator cuff muscles

Anterior view

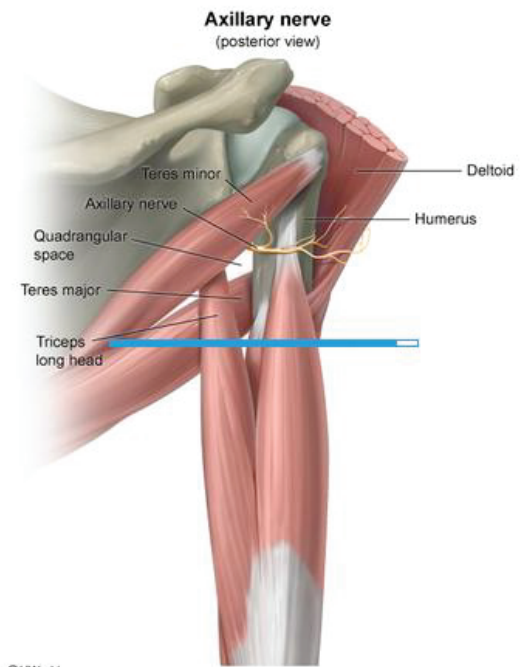
Posterior view





stacking boxes)

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 68-year-old woman comes to the emergency department due to an acute vision disturbance. She had an episode of dimming of vision in the left eye that occurred abruptly and resolved spontaneously in 20 minutes. For the past several weeks, the patient has had a dull ache in the left side of her jaw while chewing that resolves when she stops eating. She has also had malaise and hip muscle aches over the last several months. The patient has a history of hypertension and hypothyroidism. On examination, her blood pressure is 130/70 mm Hg and pulse is 66/min. Neurological examination, including cranial nerves and motor and sensory functions, is unremarkable. Visual acuity, visual fields, and appearance of the ocular fundi are normal. Which of the following is the best initial test for this patient?

- ☐ A. Angiography
- ☐ B. Blood lipid fractions
- ☐ C. Erythrocyte sedimentation rate
- ☐ D. Head CT scan
- ☐ E. Rheumatoid factor
- ☐ F. Transthoracic echocardiography



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Feedback



Suspend



End Block



minutes. For the past several weeks, the patient has had a dull ache in the left side of her jaw while chewing that resolves when she stops eating. She has also had malaise and hip muscle aches over the last several months. The patient has a history of hypertension and hypothyroidism. On examination, her blood pressure is 130/70 mm Hg and pulse is 66/min. Neurological examination, including cranial nerves and motor and sensory functions, is unremarkable. Visual acuity, visual fields, and appearance of the ocular fundi are normal. Which of the following is the best initial test for this patient?

- ☐ A. Angiography (12%)
- ☐ B. Blood lipid fractions (2%)
- ☒ C. Erythrocyte sedimentation rate (72%)
- ☐ D. Head CT scan (7%)
- ☐ E. Rheumatoid factor (3%)
- ☐ F. Transthoracic echocardiography (1%)

Correct

72%



56 secs



01/24/2021

Block Time Remaining: 00:43:49

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Feedback



Suspend



End Block

Giant cell arteritis

| | |
|------------------|--|
| Symptoms | <ul style="list-style-type: none"> • Systemic: fever, fatigue, malaise, weight loss • Headache • Jaw claudication • Visual disturbances (eg, ischemic optic neuropathy) • Polymyalgia rheumatica |
| Diagnosis | <ul style="list-style-type: none"> • Elevated erythrocyte sedimentation rate & C-reactive protein • Temporal artery biopsy: intimal thickening, elastic lamina fragmentation, multinucleated giant cells |
| Treatment | <ul style="list-style-type: none"> • Glucocorticoids |

This patient, an elderly woman with **jaw claudication** and an episode of **amaurosis fugax** (ie, transient monocular visual loss), most likely has **giant cell (temporal) arteritis** (GCA). GCA is the most common form of vasculitis in persons of northern European descent and occurs almost exclusively in patients **age >50**. About half of patients with GCA will also have **polymyalgia rheumatica**, which causes achy pain in the shoulder and hip girdles. Headache is the most common presentation of GCA, but jaw or tongue



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient, an elderly woman with **jaw claudication** and an episode of **amaurosis fugax** (ie, transient monocular visual loss), most likely has **giant cell (temporal) arteritis** (GCA). GCA is the most common form of vasculitis in persons of northern European descent and occurs almost exclusively in patients **age >50**. About half of patients with GCA will also have **polymyalgia rheumatica**, which causes achy pain in the shoulder and hip girdles. Headache is the most common presentation of GCA, but jaw or tongue claudication is also common. Ocular manifestations may include amaurosis, diplopia, blurred vision, and ischemic optic neuropathy; untreated GCA may lead to permanent blindness.

Physical findings in GCA may be normal, but patients often have tenderness over the course of the temporal artery. If GCA is suspected, a **C-reactive protein** (CRP) level or **erythrocyte sedimentation rate** (ESR) should be determined promptly. Although CRP and ESR are nonspecific, they are highly sensitive and almost always significantly elevated in GCA. Patients with characteristic symptoms and elevated CRP or ESR should undergo **temporal artery biopsy** for definitive diagnosis.

(Choice A) Angiography in GCA may show focal areas of arterial narrowing, but it is not as sensitive as ESR and CRP for initial assessment.

(Choice B) GCA is associated with an increased risk of cardiovascular events, including transient ischemic attack (TIA), stroke, and myocardial infarction. Appropriate management of other cardiovascular



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

ischemic attack (TIA), stroke, and myocardial infarction. Appropriate management of other cardiovascular risk factors (eg, hyperlipidemia) is recommended but should not delay initial evaluation.

(Choice D) Noncontrast head CT is recommended for initial evaluation of patients with TIA and stroke. However, this patient has no focal neurologic deficits, and her amaurosis and jaw claudication are more consistent with GCA.

(Choice E) In addition to elevated ESR and CRP levels, other nonspecific signs of inflammation, such as thrombocytosis, may be present in patients with GCA. However, specific serologic markers, such as rheumatoid factor, are not elevated.

(Choice F) Echocardiography is recommended for patients with a suspected cardioembolic event. Although cardioembolism may rarely present with amaurosis, this patient's other features are more characteristic of GCA.

Educational objective:

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have very high sensitivity for giant cell (temporal) arteritis. Patients with suspected giant cell arteritis who have an elevated ESR or CRP level should be referred for temporal artery biopsy to confirm the diagnosis.

References





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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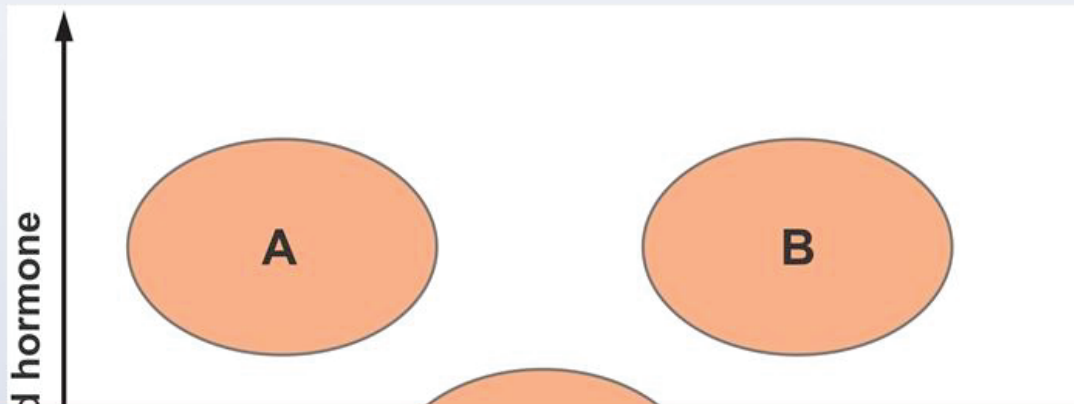


Text Zoom



Settings

A 68-year-old Caucasian woman comes to the emergency department due to several hours of severe upper back pain. The patient developed the pain after experiencing a sudden jolt while driving over a pothole. She has no previous history of back pain or major trauma and has not seen a doctor in many years. The patient is retired and lives a sedentary lifestyle. She drinks a glass of wine daily and eats a healthy, balanced diet. BMI is 18.4 kg/m^2 . On examination, there is point tenderness over the T10 vertebra. Neurologic examination is unremarkable. X-ray of the spine reveals a T10 compression fracture. On the graph, area C represent the normal serum concentrations of calcium and parathyroid hormone.



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

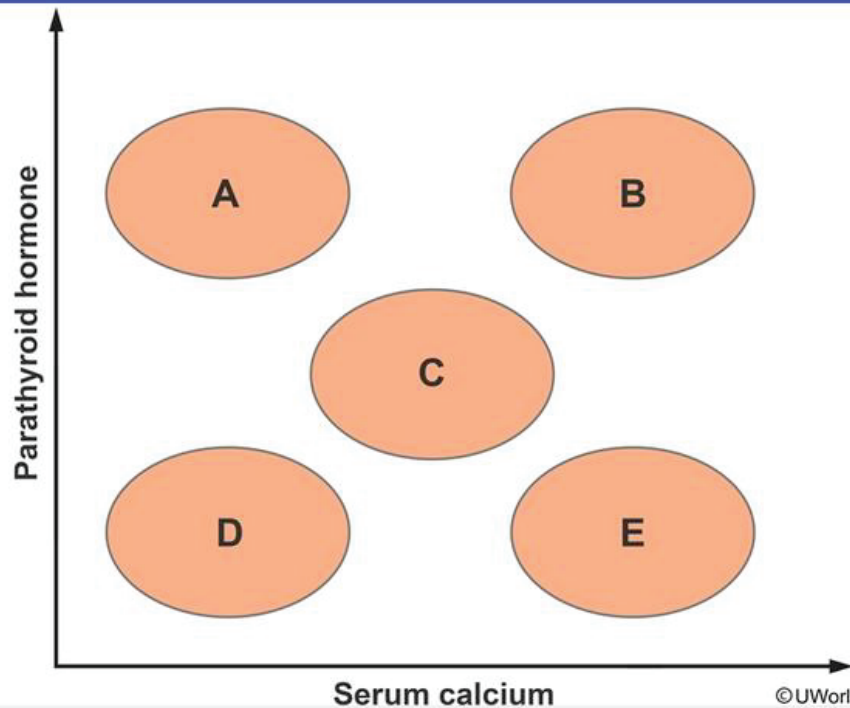


Text Zoom



Settings

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Zoom In

Zoom Out

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Feedback



Suspend



End Block



Mark

Previous

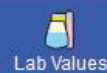
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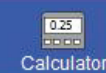
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Lab Values



Notes



Calculator



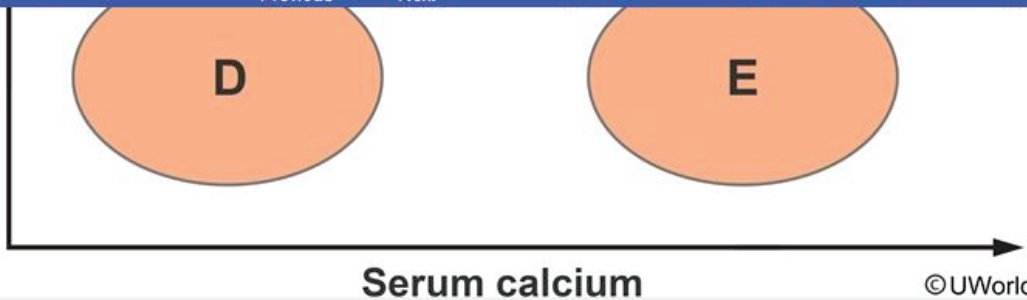
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Which of the following areas most likely corresponds to this patient's current metabolic state?

- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit

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Previous

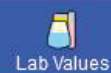
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Full Screen



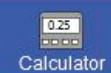
Tutorial



Lab Values



Notes



Calculator



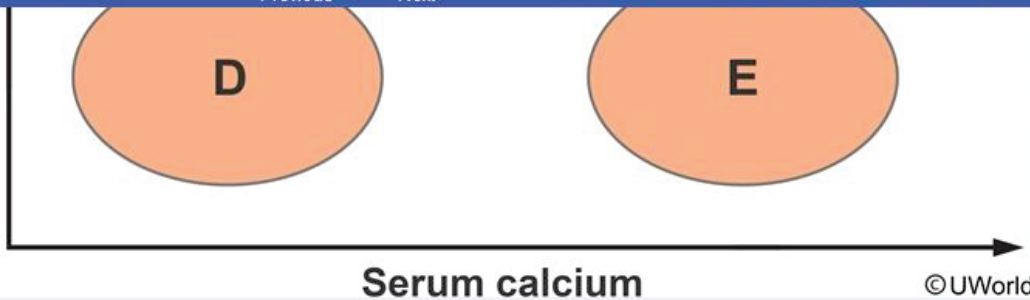
Reverse Color



Text Zoom



Settings



Which of the following areas most likely corresponds to this patient's current metabolic state?

- ☐ A.A (29%)
- ☐ B.B (9%)
- ☒ C.C (43%)
- ☐ D.D (7%)
- ☐ E.E (11%)

Correct

43%



01 min, 57 secs



09/28/2020

Block Time Remaining: 00:45:46

TUTOR

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Normal trabecular bone



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Osteoporotic bone



This patient with a thoracic compression fracture has multiple **risk factors** for **osteoporosis** (Caucasian ethnicity, female sex, postmenopausal status). Osteoporosis is characterized by decreased bone strength resulting from **low bone mass** and microarchitectural deterioration of bone tissue. The presence of a fragility fracture due to minimal trauma (eg, fall from a standing height) is strongly suggestive of osteoporosis.

Early postmenopausal osteoporosis primarily involves cancellous bone, which is especially important for



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Feedback



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End Block

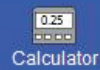
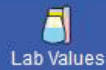


Exhibit Display

Risk factors for osteoporotic fractures

| Nonmodifiable | Potentially modifiable |
|---|---|
| <ul style="list-style-type: none">• Advancing age• Female sex• White, Hispanic, or Asian ethnicity• Personal or family history of fracture | <ul style="list-style-type: none">• Decreased physical activity• Low body weight• Poor calcium & vitamin D intake• Excessive alcohol or tobacco use• Premature menopause• Glucocorticoid use |



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This patient with a
ethnicity, female sex
resulting from **low**
fragility fracture due
osteoporosis.

Early postmenopau

⚡ New | Existing





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

osteoporosis.

Early postmenopausal osteoporosis primarily involves cancellous bone, which is especially important for maintaining the integrity of the vertebral column. Therefore, **vertebral fractures** are the most common manifestation of osteoporosis. With advancing age, the cortical bone (compact bone) that makes up the shafts of long bones and outer envelopes of all bones becomes more involved, leading to an increased risk of **hip fracture**.

In primary osteoporosis (ie, osteoporosis that is not due to an underlying medical disorder), serum calcium, phosphorus, and parathyroid hormone (PTH) levels are typically in the **normal** range.

(Choice A) High serum PTH with low serum calcium (area A in the diagram) is usually seen in patients with renal failure or vitamin D deficiency.

(Choices B and E) High calcium, high PTH (area B) is consistent with primary hyperparathyroidism. High calcium levels with low PTH (area E) would be seen in patients with PTH-independent hypercalcemia (PTH is appropriately suppressed by high calcium levels), which can occur with humoral hypercalcemia of malignancy and vitamin D toxicity.

(Choice D) In patients with hypoparathyroidism, low PTH levels cause hypocalcemia.



Feedback



Suspend



End Block



phosphorus, and parathyroid hormone (PTH) levels are typically in the normal range.

(Choice A) High serum PTH with low serum calcium (area A in the diagram) is usually seen in patients with renal failure or vitamin D deficiency.

(Choices B and E) High calcium, high PTH (area B) is consistent with primary hyperparathyroidism. High calcium levels with low PTH (area E) would be seen in patients with PTH-independent hypercalcemia (PTH is appropriately suppressed by high calcium levels), which can occur with humoral hypercalcemia of malignancy and vitamin D toxicity.

(Choice D) In patients with hypoparathyroidism, low PTH levels cause hypocalcemia.

Educational objective:

Patients with osteoporosis have low bone mass, resulting in increased susceptibility to fragility fractures (ie, those occurring with minimal or no trauma). In primary osteoporosis (not caused by a medical disorder), serum calcium, phosphorus, and parathyroid hormone levels are typically normal.

Pathophysiology

Rheumatology/Orthopedics & Sports

Osteoporosis

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 22-year-old woman comes to the office because of a 6-month history of increasing neck and low back pain that is most severe in the morning. Her pain improves as the day passes. The patient has no history of trauma, rashes, or urinary symptoms. Vital signs are within normal limits. Examination shows tenderness over the lumbosacral area and at the insertion site of the Achilles tendon. Forward flexion is reduced. This patient's symptoms are most likely attributable to upregulation of which of the following cytokines?

- ☐ A. IL-2 and interferon gamma
- ☐ B. IL-4 and interferon alpha
- ☐ C. IL-5 and tumor necrosis factor-alpha
- ☐ D. IL-10 and transforming growth factor-beta
- ☐ E. IL-17 and tumor necrosis factor-alpha

Submit

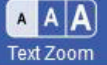
Feedback



Suspend



End Block



A 22-year-old woman comes to the office because of a 6-month history of increasing neck and low back pain that is most severe in the morning. Her pain improves as the day passes. The patient has no history of trauma, rashes, or urinary symptoms. Vital signs are within normal limits. Examination shows tenderness over the lumbosacral area and at the insertion site of the Achilles tendon. Forward flexion is reduced. This patient's symptoms are most likely attributable to upregulation of which of the following cytokines?

- ☐ A. IL-2 and interferon gamma (27%)
- ☐ B. IL-4 and interferon alpha (5%)
- ☐ C. IL-5 and tumor necrosis factor-alpha (13%)
- ☐ D. IL-10 and transforming growth factor-beta (9%)
- ☒ E. IL-17 and tumor necrosis factor-alpha (44%)

Correct

 44%
Answered correctly 02 mins, 09 secs
Time Spent 11/04/2020
Last Updated

Block Time Remaining: 00:47:55

TUTOR

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Suspend



End Block

Ankylosing spondylitis

Pathogenesis

- Altered gut biome/defective mucosal barrier
- Increased production of IL-17, TNF- α & prostaglandins
- Increased risk with HLA-B27

Clinical findings

- Inflammatory back & buttock pain
 - Insidious onset at age <40
 - Relieved with exercise but not rest
 - Nocturnal pain
- Reduced chest expansion & spinal mobility
- Enthesitis (tenderness at tendon insertion sites)
- Dactylitis (swelling of fingers & toes)
- Anterior uveitis

Laboratory/imaging

- Elevated ESR & CRP
- Sacroiliitis: bone erosions, subchondral sclerosis, eventual bony fusion (ankylosis)
- Bridging syndesmophytes: ossification at vertebral body margins



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

- Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

HLA-B27 = human leukocyte antigen B27; **TNF- α** = tumor necrosis factor-alpha; **CRP** = C-reactive protein; **ESR** = erythrocyte sedimentation rate.

This patient with **inflammatory back pain** (ie, age <40, insidious onset, worse with rest/better with activity) and **enthesitis** (ie, tenderness at insertion of tendons/ligaments on bone) most likely has **ankylosing spondylitis** (AS). AS is characterized by **bridging syndesmophytes** in the vertebral column and ankylosis (bony fusion) of the apophyseal and sacroiliac joints.

AS is an inflammatory disorder thought to originate largely in the gut:

- Defects in the mucosal barrier and an abnormal intestinal microbiome induce an IL-17-mediated inflammatory response via innate lymphoid cells and T helper cells (eg, Th1, Th17). The risk is greater in individuals with human leukocyte antigen B27 (**HLA-B27**), likely due to altered antigen presentation.
- **IL-17** stimulates production of additional inflammatory factors, primarily tumor necrosis factor-alpha (**TNF-alpha**) and **prostaglandins**, which have synergistic effects with IL-17 and induce **bony erosions** and **abnormal bone regrowth**.



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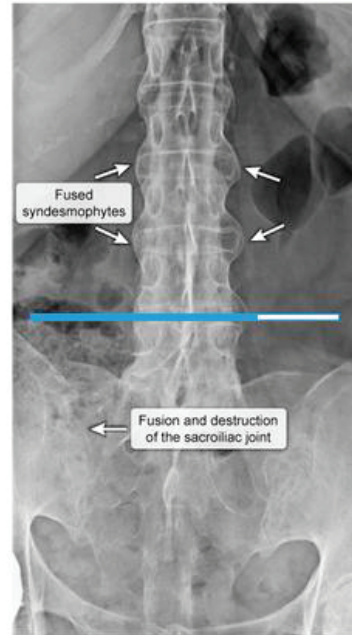
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End Block

Exhibit Display

Ankylosing spondylitis (bamboo spine)



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Skeletal manifestations of AS occur primarily at **sites of mechanical stress**, such as the entheses, likely due to the migration of activated immune cells to these areas. Treatment options include nonsteroidal anti-inflammatory drugs (eg, ibuprofen, naproxen), which inhibit prostaglandin formation, and anti-TNF-alpha (eg, etanercept, infliximab) and anti-IL-17 (eg, secukinumab) agents.

(Choice A) IL-2 and interferon gamma have broad immune functions, including activation of the response against viruses and mycobacteria. Both cytokines inhibit Th17 cell differentiation and do not have a significant role in the pathogenesis of AS.

(Choice B) IL-4 is important in the differentiation of naïve Th cells into the Th2 subset, alternative macrophage activation (M2 type), and IgE production. It may also have a protective role in AS by limiting IL-17 production by Th1 and Th17 cells. Interferon alpha is involved primarily in antiviral activity and is not a significant factor in the pathogenesis of AS.

(Choice C) IL-5 induces B-cell growth, IgA production, and eosinophil activity. IL-5 and IL-4 are important in the etiology of certain allergic disorders (eg, allergic rhinitis, asthma), but do not contribute significantly to AS.

(Choice D) IL-10 is an antiinflammatory cytokine. Transforming growth factor-beta has antiinflammatory and immunosuppressive effects. These cytokines have only a minor effect in AS.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) IL-4 is important in the differentiation of naïve Th cells into the Th2 subset, alternative macrophage activation (M2 type), and IgE production. It may also have a protective role in AS by limiting IL-17 production by Th1 and Th17 cells. Interferon alpha is involved primarily in antiviral activity and is not a significant factor in the pathogenesis of AS.

(Choice C) IL-5 induces B-cell growth, IgA production, and eosinophil activity. IL-5 and IL-4 are important in the etiology of certain allergic disorders (eg, allergic rhinitis, asthma), but do not contribute significantly to AS.

(Choice D) IL-10 is an antiinflammatory cytokine. Transforming growth factor-beta has antiinflammatory and profibrotic effects. These cytokines have only a minor effect in AS.

Educational objective:

The pathogenesis of ankylosing spondylitis likely originates with defects in the intestinal mucosal barrier and exposure to the gut microbiome that lead to an enhanced IL-17-mediated inflammatory response. IL-17 stimulates production of additional inflammatory factors, primarily tumor necrosis factor-alpha and prostaglandins, which have synergistic proinflammatory effects and induce bony erosions and abnormal bone regrowth in the skeleton.



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 38-year-old man comes to the office due to a 2-month history of an enlarging, localized swelling on the left foot. Tying his shoelaces too tight leads to localized pain and numbness in the third and fourth toes. Examination shows a firm, nontender, well-circumscribed lesion on the dorsum of the foot as shown in the [exhibit](#). The lesion transilluminates when a penlight is applied to it. Without treatment, which of the following is most likely to occur in this patient?

- ☐ A. Bloodstream infection
- ☐ B. Continued crystal aggregation
- ☐ C. Foot paralysis
- ☐ D. Malignant proliferation
- ☐ E. Spontaneous resolution

Submit

1



Feedback

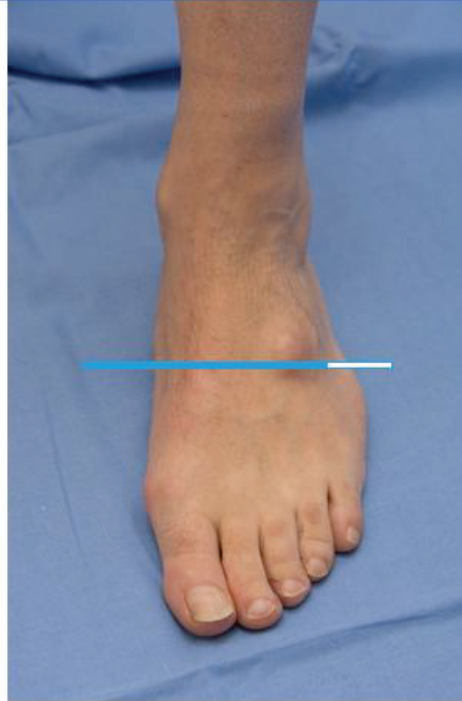


Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

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A 38-year-old man comes to the office due to a 2-month history of an **enlarging**, localized swelling on the left foot. Tying his shoelaces too tight leads to localized pain and numbness in the third and fourth toes. Examination shows a firm, nontender, well-circumscribed lesion on the dorsum of the foot as shown in the **exhibit**. The lesion **transilluminates** when a penlight is applied to it. Without treatment, which of the following is most likely to occur in this patient?

- ☐ A. Bloodstream infection (2%)
- ☐ B. Continued crystal aggregation (7%)
- ☐ C. Foot paralysis (10%)
- ☐ D. Malignant proliferation (2%)
- ☒ E. Spontaneous resolution (77%)

Correct

 77%
Answered correctly 57 secs
Time Spent 01/05/2021
Last Updated

Ganglion cyst

Pathophysiology

- Mucoid degeneration of periarticular tissue
- Herniation of connective tissue from joint capsule, tendon sheath, bursae
- Filled with clear/gelatinous fluid

Presentation

- Wrist (most common), dorsal foot, knee
- Rubbery, round, well-circumscribed cystic nodule
- Transillumination positive

Treatment

- Observation for asymptomatic cysts
- Needle aspiration (recurrence common)
- Surgical excision

Prognosis

- Most resolve spontaneously

This patient has a **ganglion cyst**, an outpouching of connective tissue arising from **tendon sheaths, joint structures** (eg, joint capsule), or bursae. Clear mucinous or **gelatinous fluid** accumulates in the sac, giving rise to a round, well-circumscribed, firm cyst that **transilluminates** on penlight examination.



This patient has a **ganglion cyst**, an outpouching of connective tissue arising from **tendon sheaths, joint structures** (eg, joint capsule), or bursae. Clear mucinous or **gelatinous fluid** accumulates in the sac, giving rise to a round, well-circumscribed, firm cyst that **transilluminates** on penlight examination. Ganglion cysts are most common on the dorsal and volar wrists, but dorsal foot lesions are also common.

Most ganglion cysts **resolve spontaneously** and do not require specific treatment. Cysts that raise cosmetic concerns or cause pain or paresthesia (due to nerve compression) can be treated with needle aspiration if desired. However, recurrence is common, and patients may eventually require surgical excision.

(Choice A) Bloodstream infection (bacteremia) can be a complication of **cutaneous abscess**, which also presents as localized swelling. Unlike a ganglion cyst, an abscess is red, painful, and fluctuant on palpation. Because of the collection of pus (an opaque liquid), an abscess does not transilluminate.

(Choice B) **Gouty tophi** are hard, irregular, subcutaneous collections of uric acid crystals found in patients with gout. Because of its solid nature, a gouty tophus does not transilluminate.

(Choice C) This patient's ganglion cyst is causing compression of dorsal cutaneous nerves (sensory branches of **superficial peroneal nerve**), leading to paresthesia. However, these branches do not contain motor fibers and so the patient is not at risk for paralysis.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

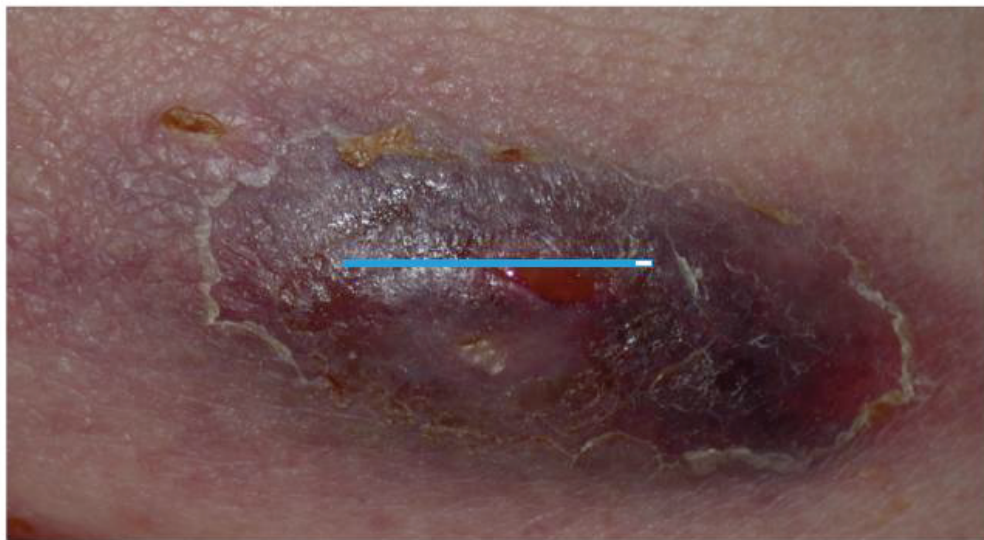
Text Zoom

Settings

This patient has a **ganglion cyst**, an outpouching of connective tissue arising from tendon sheath, joint

Exhibit Display

Cutaneous abscess



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New | Existing

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1



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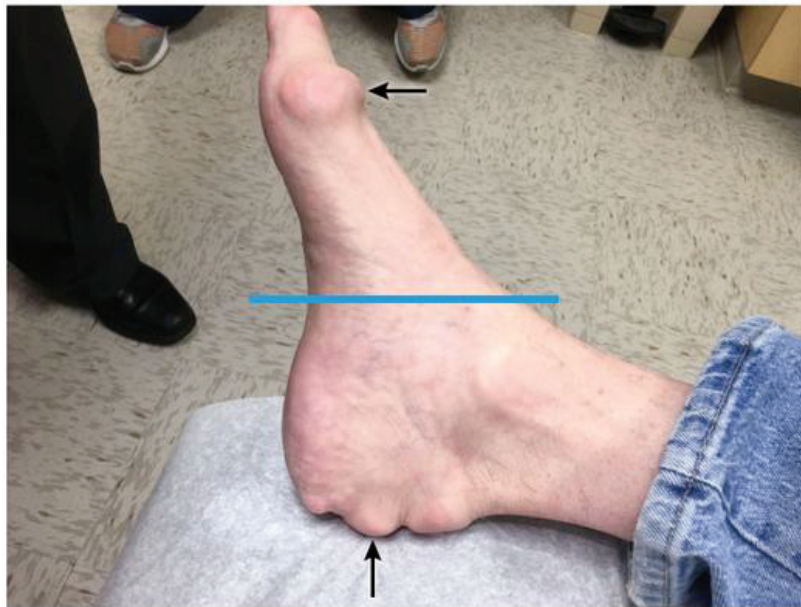


End Block

This patient has a condition associated with an outpouching of connective tissue arising from tendon sheaths of the joint.

Exhibit Display

Gouty tophi



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Zoom In

Zoom Out

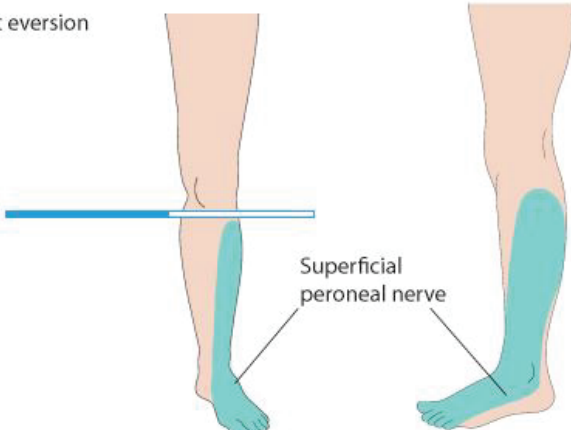
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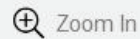
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This patient has a ganglion cyst, an outpouching of connective tissue arising from tendon sheath, joint

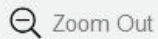
Exhibit Display

| Nerve | Motor function | Cutaneous innervation |
|----------------------------|----------------|--|
| Superficial peroneal nerve | Foot eversion |  |

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Zoom Out



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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

palpation. Because of the collection of pus (an opaque liquid), an abscess does not transilluminate.

(Choice B) **Gouty tophi** are hard, irregular, subcutaneous collections of uric acid crystals found in patients with gout. Because of its solid nature, a gouty tophus does not transilluminate.

(Choice C) This patient's ganglion cyst is causing compression of dorsal cutaneous nerves (sensory branches of **superficial peroneal nerve**), leading to paresthesia. However, these branches do not contain motor fibers and so the patient is not at risk for paralysis.

(Choice D) Synovial sarcoma can present as a mass adjacent to a joint in a young adult; however, due to its solid nature, it does not transilluminate.

Educational objective:

A ganglion cyst is a connective tissue outpouching arising from tendon sheaths and joint structures. It is typically round, firm, well-circumscribed, and transilluminates on penlight examination. Most resolve spontaneously.

References

- **Treatment of ganglion cysts.**





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



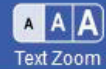
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 68-year-old woman comes to the emergency department due to pain in the left upper arm after a fall from standing height. Medical history is significant for hypothyroidism and hypertension. Physical examination shows bruising of the shoulder. Left arm movement is limited due to pain. Plain radiographs reveal a nondisplaced left humerus fracture at the anatomical neck. This patient is at greatest risk for which of the following complications?

- ☐ A. Biceps tendon rupture
- ☐ B. Brachial artery tear
- ☐ C. Humeral head necrosis
- ☐ D. Median nerve injury
- ☐ E. Radial nerve palsy

Submit

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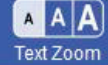
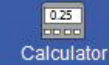
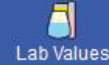
Feedback



Suspend




End Block



A 68-year-old woman comes to the emergency department due to pain in the left upper arm after a fall from standing height. Medical history is significant for **hypothyroidism** and hypertension. Physical examination shows bruising of the shoulder. Left arm movement is limited due to pain. Plain radiographs reveal a nondisplaced **left humerus fracture** at the **anatomical neck**. This patient is at greatest risk for which of the following complications?

- ☐ A. Biceps tendon rupture (9%)
- ☐ B. Brachial artery tear (12%)
- ☒ C. Humeral head necrosis (53%)
- ☐ D. Median nerve injury (6%)
- ☐ E. Radial nerve palsy (17%)

Correct

 53%
Answered correctly

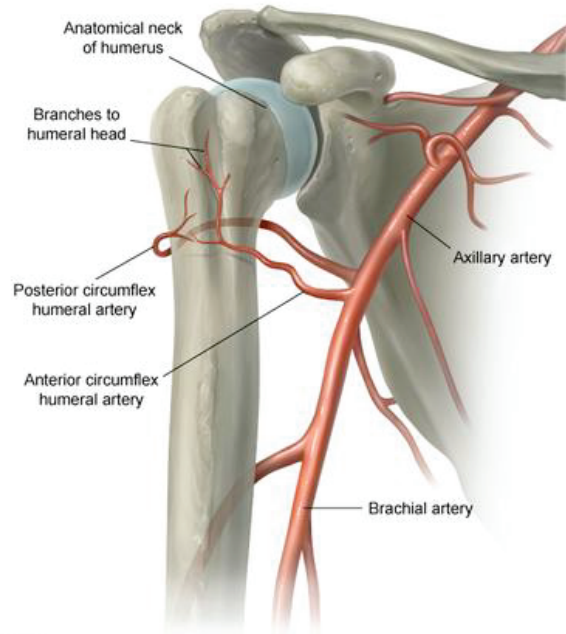
 47 secs
Time Spent

 01/31/2021
Last Updated



Exhibit Display

Circumflex humeral arteries



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient suffered a fracture of the proximal humerus at the anatomical neck. **Humeral neck fractures** commonly occur in falls; risk factors include age >65 and osteoporosis. They often occur as isolated injuries but may also be associated with glenohumeral dislocation.

The proximal humerus and glenohumeral joint receive their blood supply via the **anterior and posterior circumflex humeral arteries**, which are branches of the axillary artery that form an anastomosis encircling the neck of the humerus in the **quadrangular space**. This anastomosis gives rise to intraosseous arteries that travel back to the humeral head; humeral neck fractures can disrupt this **retrograde blood flow**, leading to **avascular necrosis** (osteonecrosis) of the humeral head. Osteonecrosis presents insidiously with shoulder pain, decreased range of motion, and flattening of the humeral head on x-ray.

(Choice A) Biceps tendon rupture presents with weakness of shoulder flexion and a noticeable bulge in the anterior arm. It most commonly occurs due to chronic overuse tendinopathy or acute forceful contraction of the biceps, but humeral neck fracture does not usually disrupt the tendon.

(Choices B and D) **Supracondylar fracture** may injure the brachial artery and median nerve where they pass anterior to the distal humerus. These structures are not at risk from proximal humerus fracture.

(Choice E) The **radial nerve** and deep brachial artery run posterior to the midshaft of the humerus and may be injured by a fracture at that point. These structures are not typically injured in a humeral neck



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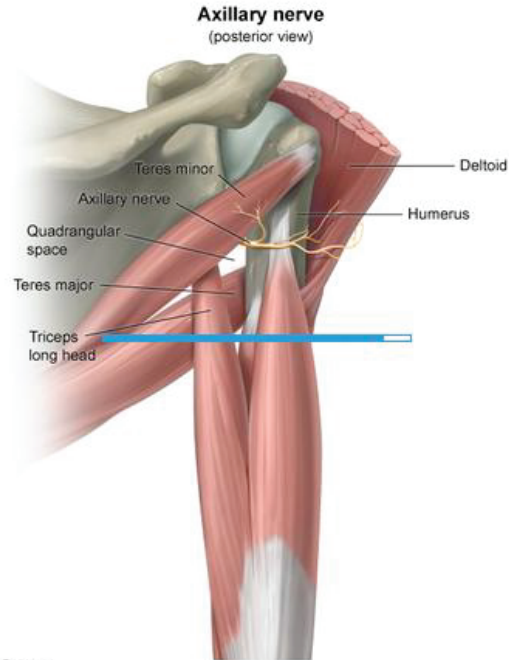


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End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



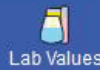
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Full Screen



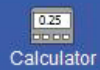
Tutorial



Lab Values



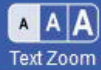
Notes



Calculator



Reverse Color



Text Zoom

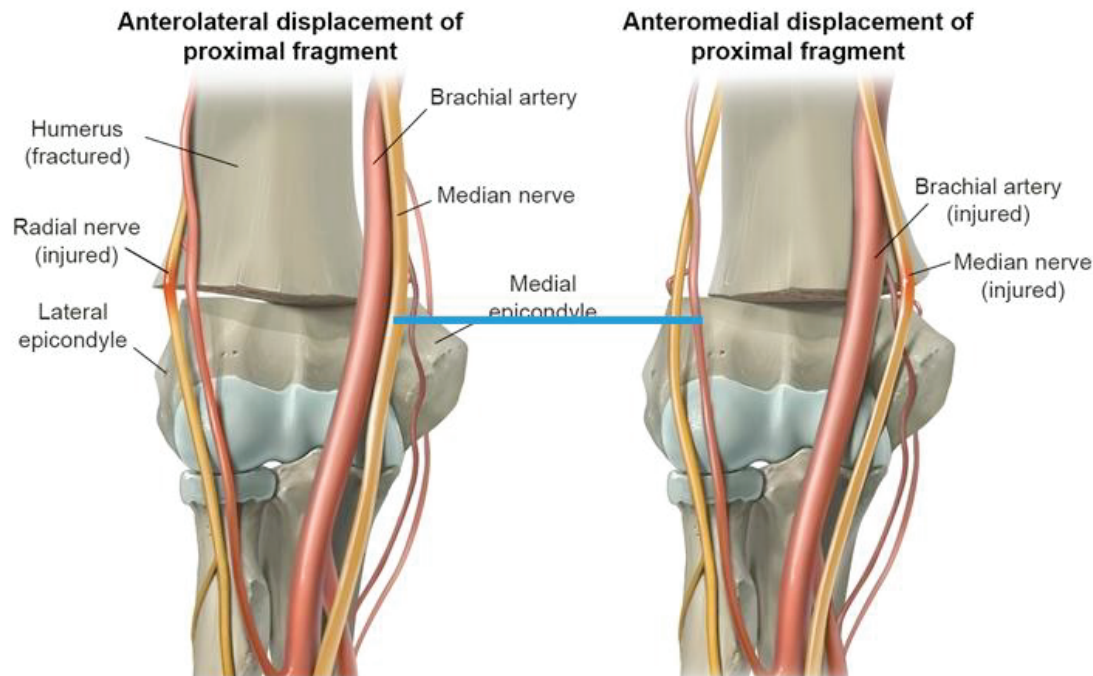


Settings

Exhibit Display

[Supracondylar fracture](#) Supracondylar fracture

Supracondylar humeral fracture



Zoom In

Zoom Out

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New | Existing

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Block Time Remaining: 00:49:40

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Feedback

Suspend

End Block



(Choice A) Biceps tendon rupture presents with weakness of shoulder flexion and a noticeable bulge in the anterior arm. It most commonly occurs due to chronic overuse tendinopathy or acute forceful contraction of the biceps, but humeral neck fracture does not usually disrupt the tendon.

(Choices B and D) **Supracondylar fracture** may injure the brachial artery and median nerve where they pass anterior to the distal humerus. These structures are not at risk from proximal humerus fracture.

(Choice E) The **radial nerve** and deep brachial artery run posterior to the midshaft of the humerus and may be injured by a fracture at that point. These structures are not typically injured in a humeral neck fracture.

Educational objective:

The proximal humerus and glenohumeral joint receive their blood supply via the anterior and posterior circumflex humeral arteries, which are branches of the axillary artery that form an anastomosis at the neck of the humerus. Humeral neck fractures can disrupt this blood flow, leading to avascular necrosis of the humeral head.

Anatomy

Rheumatology/Orthopedics & Sports

Upper extremity long bone fracture

Subject

System

Topic

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Block Time Remaining: 00:49:40

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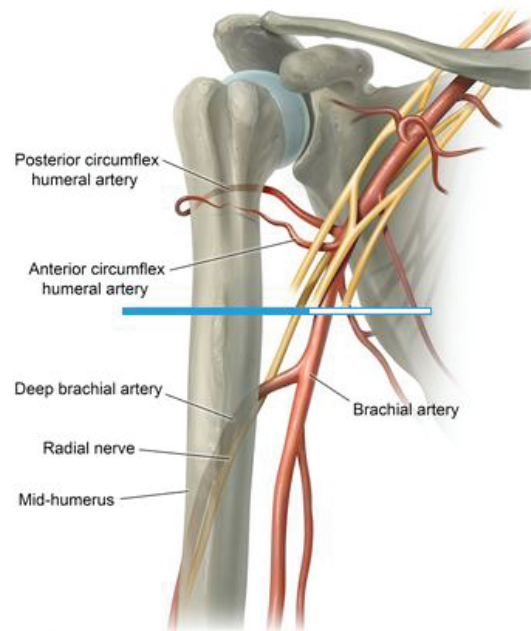
Suspend

End Block

(Choice A) Biceps tendon rupture presents with weakness of shoulder flexion and a noticeable bulge in

Exhibit Display

Deep brachial artery & radial nerve



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A 29-year-old previously healthy man comes to the hospital with a right leg injury after a cycling accident. He reports pain in the lower leg and inability to bear weight. X-ray reveals right tibial and fibular shaft fractures. The patient undergoes closed reduction and immobilization of the fractures. Several hours later, he has increasingly severe pain in his right leg. Physical examination shows increased tension within the anterior compartment. Which of the following structures is most likely to be compromised by this patient's acute complication?

- ☐ A. Deep peroneal nerve
- ☐ B. Great saphenous vein
- ☐ C. Peroneal veins
- ☐ D. Posterior tibial artery
- ☐ E. Superficial peroneal nerve
- ☐ F. Tibial nerve

Submit

Block Time Remaining: 00:49:42

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Feedback

Suspend

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 29-year-old previously healthy man comes to the hospital with a right leg injury after a cycling accident. He reports pain in the lower leg and inability to bear weight. X-ray reveals **right tibial** and **fibular shaft** fractures. The patient undergoes closed reduction and immobilization of the fractures. Several hours later, he has increasingly severe pain in his right leg. Physical examination shows increased tension within the **anterior compartment**. Which of the following structures is most likely to be compromised by this patient's acute complication?

- ☒ A. Deep peroneal nerve (40%)
- ☐ B. Great saphenous vein (6%)
- ☐ C. Peroneal veins (7%)
- ☐ D. Posterior tibial artery (6%)
- ☐ E. Superficial peroneal nerve (24%)
- ☐ F. Tibial nerve (14%)



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Feedback



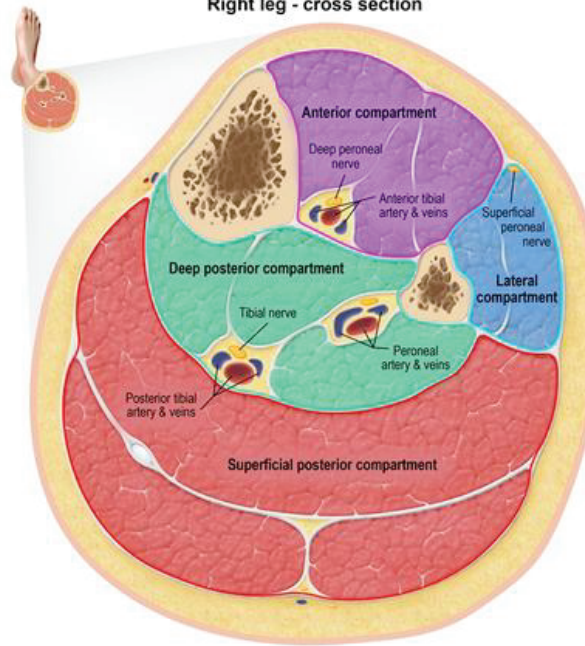
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Right leg - cross section



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The deep fascia of the leg, the fascial intermuscular septae, and the interosseous membrane divide the leg into 4 compartments (anterior, lateral, and superficial and deep posterior). The fascia is inelastic and limits outward expansion of the contracting muscles. If the pressure in a compartment increases, the circulation within it can become compromised, leading to severe pain and eventual tissue ischemia. This complication, **acute compartment syndrome** (ACS), can be due to long-bone fractures, crush injury, thermal injury, or nontraumatic causes (eg, bleeding disorders, vascular disease). Early diagnosis and surgical decompression (fasciotomy) of the involved compartments are necessary to prevent permanent and disabling injury (eg, myonecrosis, nerve damage, amputation).

The most common site for ACS is the **anterior compartment** of the leg, which includes the foot extensor muscles, **anterior tibial artery**, and the **deep peroneal (fibular) nerve**. Injury to the deep peroneal nerve causes decreased sensation between the first and second toes, decreased dorsiflexion of the foot, foot drop, and claw foot.

(Choice B) The great (long) saphenous vein starts in the dorsum of the foot and runs along the medial leg and anterior thigh before merging with the common femoral vein in the femoral triangle. It is outside the deep fascia and is not vulnerable to ACS.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice C) The peroneal veins accompany the peroneal artery and drain blood from the lateral compartment into the deep posterior compartment and eventually into the posterior tibial veins.

(Choices D and F) The deep posterior compartment contains the posterior tibial artery, peroneal artery, and tibial nerve. ACS involving this compartment may cause decreased sensation in the plantar surface, decreased toe flexion, and pain with passive toe extension.

(Choice E) The lateral compartment of the leg contains the superficial peroneal nerve and the proximal part of the deep peroneal nerve. ACS in this compartment can produce loss of sensation in the lower leg and dorsum of the foot as well as foot drop.

Educational objective:

Acute compartment syndrome (ACS) is caused by increased pressure within fascial compartments of the limbs, leading to impaired perfusion. ACS can cause severe pain, myonecrosis, and nerve injury. The anterior compartment of the leg, which contains the deep peroneal (fibular) nerve, is the most common site of ACS.

References

- [Acute lower-leg compartment syndrome.](#)



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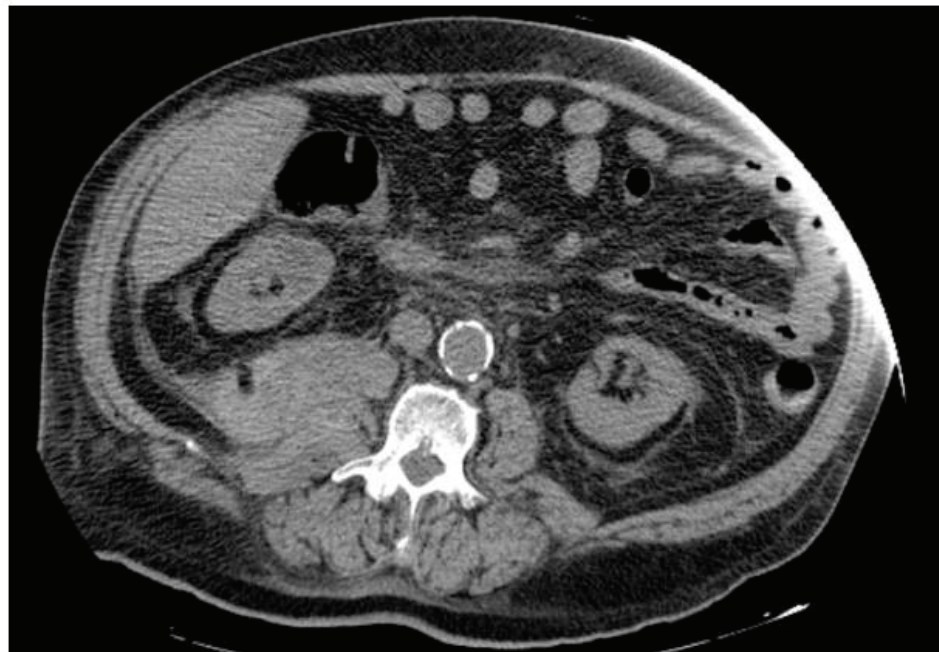


End Block

A 65-year-old man comes to the office due to right lower abdominal pain that radiates to his groin and difficulty walking for the past week. Climbing stairs has been particularly hard for him, and he has fallen several times due to knee buckling. Medical history is significant for diabetes mellitus, hypertension, and atrial fibrillation. The patient takes warfarin for chronic anticoagulation. On physical examination, the right patellar reflex is decreased compared to the left. Abdominal CT scan is shown below:



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Which of the following additional findings is most likely to be seen in this patient?

- ☐ A. Impaired adduction of the right thigh
- ☐ B. Loss of sensation on the anterior aspect of the right thigh
- ☐ C. Loss of sensation on the dorsum of the right foot
- ☐ D. Loss of sensation on the sole of the right foot
- ☐ E. Weakened abduction of the right thigh

Submit



Which of the following additional findings is most likely to be seen in this patient?

- ☐ A. Impaired adduction of the right thigh (15%)
- ☒ B. Loss of sensation on the anterior aspect of the right thigh (51%)
- ☐ C. Loss of sensation on the dorsum of the right foot (10%)
- ☐ D. Loss of sensation on the sole of the right foot (5%)
- ☐ E. Weakened abduction of the right thigh (16%)

Correct

51%
Answered correctly

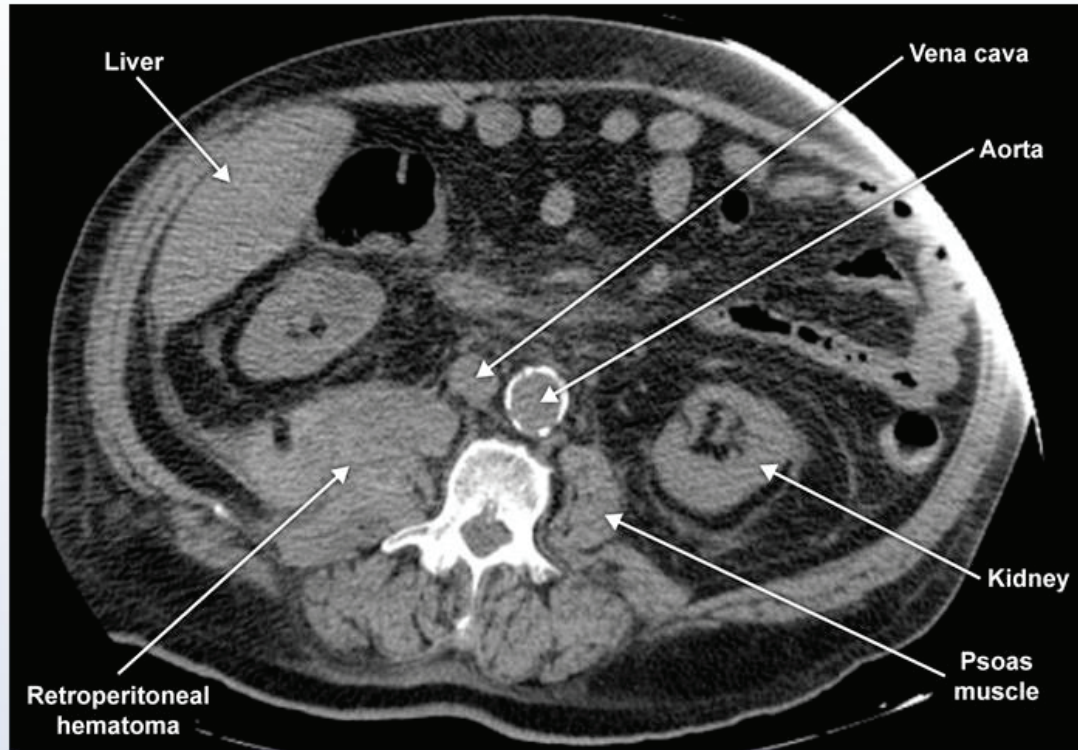
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01/03/2021
Last Updated


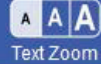
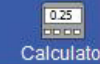
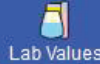
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This patient's CT scan reveals a large fluid collection in the right retroperitoneum anterior to the psoas



Retroperitoneal
hematoma

This patient's CT scan reveals a large fluid collection in the right retroperitoneum anterior to the psoas muscle. The fluid is isodense compared with muscle and displaces the right kidney. These findings are consistent with a spontaneous **retroperitoneal hematoma**, which occurs most often in patients receiving anticoagulation therapy (eg, warfarin). Affected patients often present with acute, severe pain in the groin, lower abdomen, or back; injury to the femoral nerve can also occur due to its proximity.

The **femoral nerve** descends through the psoas major muscle, emerges laterally between the psoas and iliacus muscle, and then runs beneath the inguinal ligament into the thigh. **Femoral nerve mononeuropathy** can occur due to trauma (eg, pelvic fracture), **compression from a hematoma** or abscess, or injury during surgery/childbirth. Findings of femoral neuropathy include **quadriceps weakness** (eg, difficulty with stairs, falling due to knee buckling), **decreased patellar reflex**, and **sensory loss** over the **anterior and medial thigh** and medial leg.





(Choice A) Obturator nerve injury presents with weakness of thigh adduction and medial thigh sensory loss. It is most commonly seen as an iatrogenic complication of pelvic surgery.

(Choice C) Peroneal nerve injury often presents with loss of dorsal foot sensation and foot drop due to weakness of foot eversion, dorsiflexion, and toe extension. It is typically caused by **compression of the**



Retroperitoneal

Exhibit Display

| Lower extremity nerve | Nerve roots | Cause of injury | Sensory deficit | Motor deficit |
|-----------------------|-------------|--|---|---|
| Obturator | L2-L4 | Iatrogenic (eg, pelvic surgery) |  | Thigh adduction |
| Femoral | L2-L4 | Pelvic fracture or mass involving iliopsoas/iliacus muscle (eg, hematoma or abscess) |  | Flexion of thigh, extension of leg |
| Common peroneal | L4-S2 | Fibula neck fracture or nerve compression at fibular neck |  | Foot eversion, dorsiflexion, toe extension |
| Tibial | L4-S3 | Trauma to the knee, tarsal tunnel syndrome |  | Foot inversion, plantar flexion & toe flexion |
| Superior gluteal | L4-S1 | Iatrogenic (eg, posterior hip dislocation or buttocks injection) | None | Thigh abduction |
| Inferior gluteal | L5-S2 | | None | Thigh extension |

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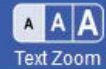
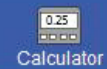
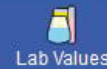
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thigh and medial leg.

(Choice A) Obturator nerve injury presents with weakness of thigh adduction and medial thigh sensory loss. It is most commonly seen as an iatrogenic complication of pelvic surgery.

(Choice C) Peroneal nerve injury often presents with loss of dorsal foot sensation and foot drop due to weakness of foot eversion, dorsiflexion, and toe extension. It is typically caused by **compression of the nerve** at the proximal fibula (eg, from leg casting).

(Choice D) Tibial nerve injury causes numbness at the sole and is typically associated with decreased inversion and plantarflexion of the foot and flexion of the toes. Common causes include knee trauma and tarsal tunnel syndrome.

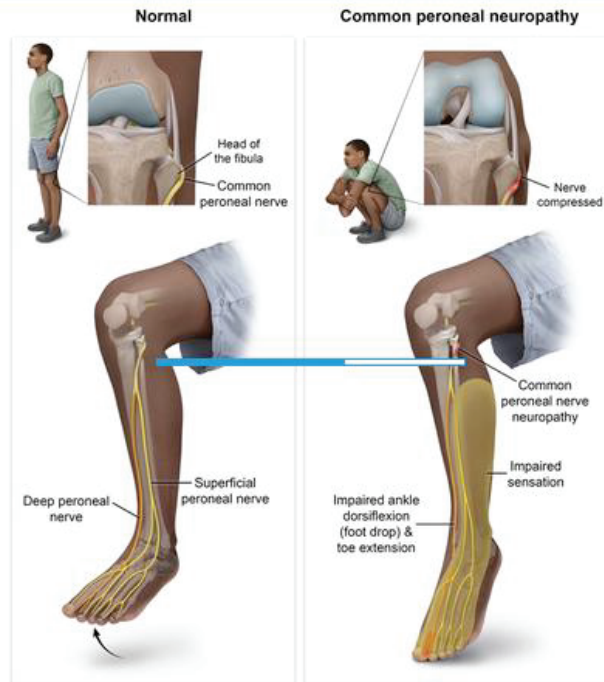
(Choice E) Weakened abduction of the thigh occurs with superior gluteal nerve injury and results in a **Trendelenburg gait**. There are no associated sensory deficits.

Educational objective:

Femoral nerve mononeuropathy can occur due to trauma; compression from a retroperitoneal hematoma or abscess, or injury during surgery or childbirth. Findings include quadriceps weakness, decreased patellar reflex, and sensory loss over the anterior and medial thigh and medial leg.



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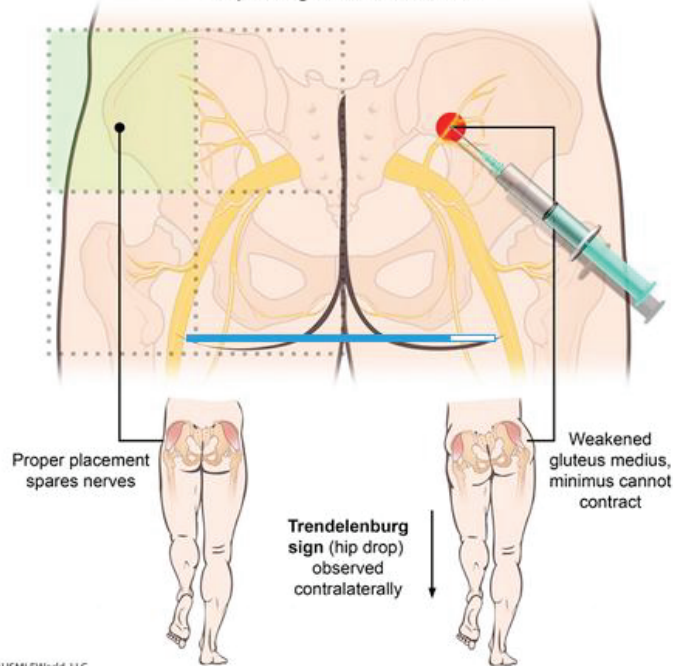


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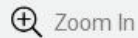
Anatomy and Physiology

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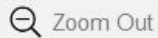
Superior gluteal nerve lesion



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1



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Previous



Next



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Notes



Calculator



Reverse Color



Text Zoom



Settings

A 43-year-old man comes to the office due to difficulty walking. The patient was seen at an outpatient clinic 2 days ago and received a right-sided deep intramuscular injection. He had no trouble walking at the time of the appointment but started having problems later that day. The patient has no history of trauma or pain at the injection site. Physical examination is negative for local erythema and swelling, and the patient has full strength against resistance on knee flexion and ankle plantar flexion bilaterally. When the patient is asked to walk across the room, his left hip drops every time he raises his left foot. Which of the following locations is the most likely site of this patient's intramuscular injection?

- ☐ A. Inferolateral quadrant of the buttock
- ☐ B. Inferomedial quadrant of the buttock
- ☒ C. Superior portion of the posterior thigh
- ☐ D. Superolateral quadrant of the buttock
- ☐ E. Superomedial quadrant of the buttock

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Block Time Remaining: 00:53:19

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1



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Previous



Next



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Notes



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Settings

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- ☐ A. Inferolateral quadrant of the buttock (8%)
- ☐ B. Inferomedial quadrant of the buttock (16%)
- ☐ C. Superior portion of the posterior thigh (0%)
- ☐ D. Superolateral quadrant of the buttock (23%)
- ☒ E. Superomedial quadrant of the buttock (51%)



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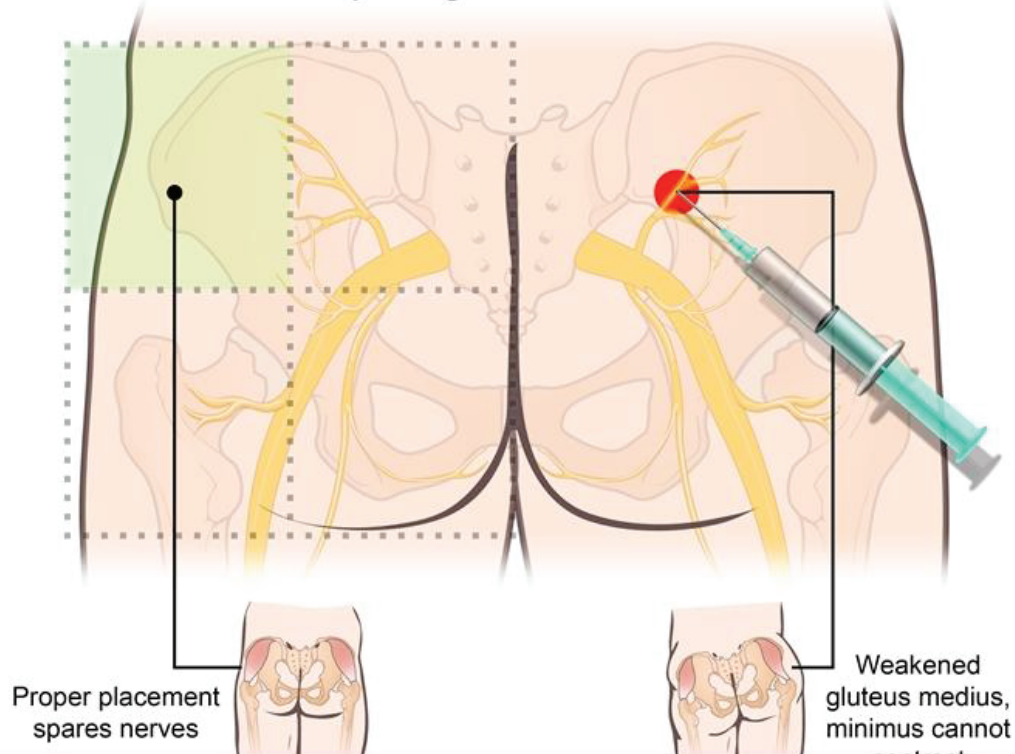


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Superior gluteal nerve lesion



Proper placement
spares nerves

Weakened
gluteus medius,
minimus cannot
contract



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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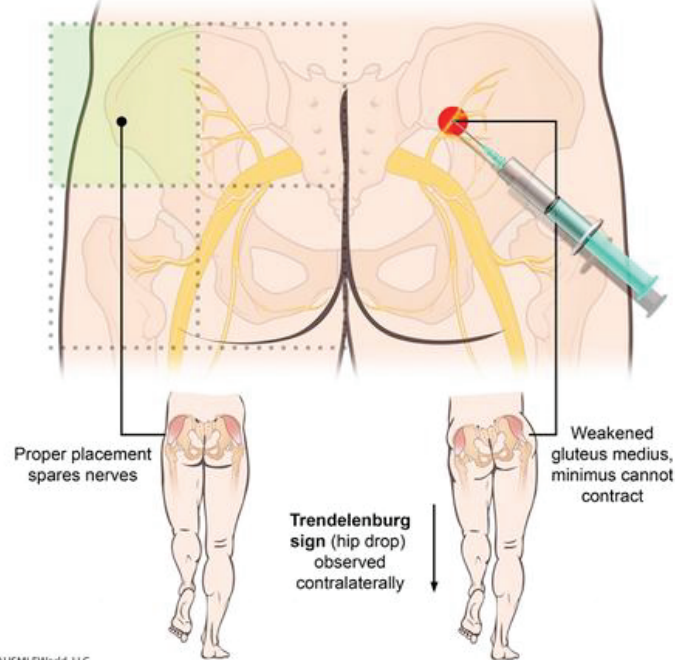
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Superior gluteal nerve lesion



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1



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Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient is exhibiting classic **Trendelenburg gait** (ie, gluteus medius gait), which is characterized by hip drop on the contralateral, unaffected side when that foot is raised. This gait is observed when there is **injury to the superior gluteal nerve** or to the gluteus medius muscle. The superior gluteal nerve is derived from the L4-S1 ventral rami and leaves the pelvis through the greater sciatic foramen above the level of the piriformis. Injections into the **superomedial quadrant** of the buttock have a high probability of injuring the superior gluteal nerve.

(Choices A, B, and C) Due to its large size, the sciatic nerve is at risk of injury following an injection in any quadrant of the buttock or the superior portion of the posterior thigh. However, the sciatic nerve innervates the knee flexors (eg, hamstrings) and leg/foot muscles, and injury to the nerve would cause weakness in knee flexion and ankle plantarflexion (eg, foot drop) rather than Trendelenburg gait.

(Choice D) The superolateral quadrant of the buttocks is considered the safest place for dorsogluteal injections. However, damage to the gluteal and sciatic nerves can still result from injections into this region. Most intragluteal injections should target the anterolateral gluteal area (ie, [von Hochstetter triangle](#)) to minimize the possibility of nerve damage.

Educational objective:

Injections given in the superomedial quadrant of the buttock have a high risk of injuring the superior gluteal



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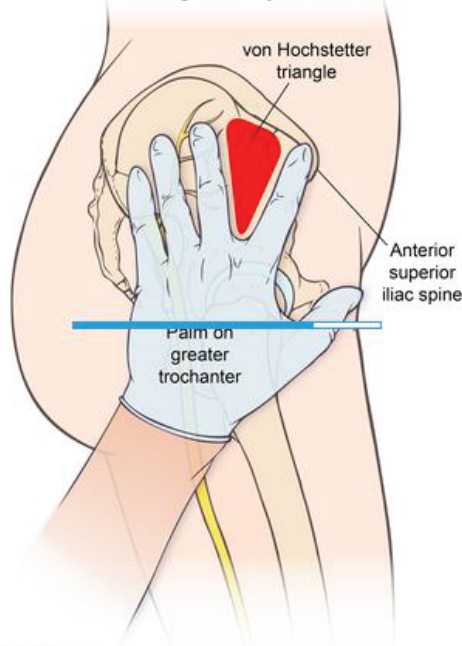
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Ventrogluteal injection site



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New | Existing

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choices A, B, and C) Due to its large size, the sciatic nerve is at risk of injury following an injection in any quadrant of the buttock or the superior portion of the posterior thigh. However, the sciatic nerve innervates the knee flexors (eg, hamstrings) and leg/foot muscles, and injury to the nerve would cause weakness in knee flexion and ankle plantarflexion (eg, foot drop) rather than Trendelenburg gait.

(Choice D) The superolateral quadrant of the buttocks is considered the safest place for dorsogluteal injections. However, damage to the gluteal and sciatic nerves can still result from injections into this region. Most intragluteal injections should target the anterolateral gluteal area (ie, [von Hochstetter triangle](#)) to minimize the possibility of nerve damage.

Educational objective:

Injections given in the superomedial quadrant of the buttock have a high risk of injuring the superior gluteal nerve, resulting in gluteus medius weakness and Trendelenburg gait. The superolateral quadrant of the buttock is a relatively safe site for intragluteal injections, although the anterolateral gluteal region is preferred.

References

- [Injection nerve palsy.](#)
- [Sciatic nerve injury from intramuscular injection: a persistent and global problem](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 36-year-old man is evaluated due to swelling and severe pain of the right foot. Medical history is significant for kidney transplant due to focal segmental glomerulosclerosis. The patient is diagnosed with gout and treated with prednisone. Six weeks later, the patient is seen at follow-up. He has no foot pain and the swelling has subsided. Serum uric acid level is 13.5 mg/dL and creatinine level is 0.9 mg/dL. Allopurinol is prescribed. Initiation of this drug would most likely increase the activity of which of the following medications?

- ☐ A. Azathioprine
- ☐ B. Ganciclovir
- ☐ C. Prednisone
- ☐ D. Tacrolimus
- ☐ E. Trimethoprim

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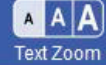
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- ☒ A. Azathioprine (85%)
- ☐ B. Ganciclovir (2%)
- ☐ C. Prednisone (1%)
- ☐ D. Tacrolimus (4%)
- ☐ E. Trimethoprim (5%)

Correct

 85%
Answered correctly 25 secs
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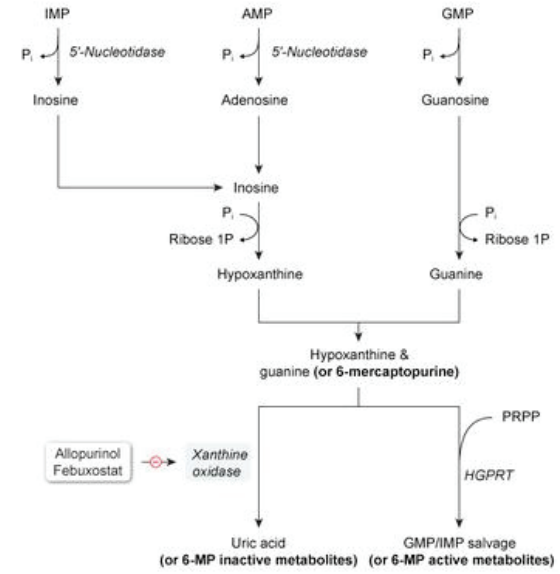
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Purine salvage pathway & 6-mercaptopurine metabolism



6-MP = 6-mercaptopurine; GMP = guanosine monophosphate; HGPRT = hypoxanthine-guanine phosphoribosyltransferase; IMP = inosine monophosphate; P_i = inorganic phosphate; PRPP = phosphoribosylpyrophosphate; Ribose 1P = ribose-1-phosphate.



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

phosphoribosyltransferase, **IMP** = inosine monophosphate, **PI** = inorganic phosphate,
PRPP = phosphoribosylpyrophosphate; **Ribose 1P** = ribose-1-phosphate.

In the purine degradation pathway, **purine bases** (ie, hypoxanthine, guanine) can follow 1 of 2 routes:

- Approximately 10% are **converted** by xanthine oxidase to **uric acid**, which is released into the bloodstream and excreted in the urine.
- The other 90% are recycled into purine nucleotides by hypoxanthine-guanine phosphoribosyltransferase (HGPRT) to be reused in the formation of DNA and RNA (ie, purine salvage).

Gout occurs due to elevated serum uric acid levels, leading to the formation of inflammation-inducing uric acid crystals within joints (eg, metatarsals). **Xanthine oxidase inhibitors** (eg, allopurinol, febuxostat) treat gout by **reducing uric acid** levels and in the process **shunt** additional **purine bases toward the salvage route**.

Azathioprine is an immunosuppression drug that is **metabolized** via the **purine degradation pathway**.

Following ingestion, **azathioprine** is converted to 6-mercaptopurine (6-MP), which is a false purine base that, like hypoxanthine and guanine, can follow 1 of 2 routes. Some 6-MP is converted by xanthine oxidase (or thiopurine methyltransferase) into inactive metabolites that are excreted in the urine. The remainder is converted by HGPRT into active metabolites (6-thioguanines), which act as false nucleotides that





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

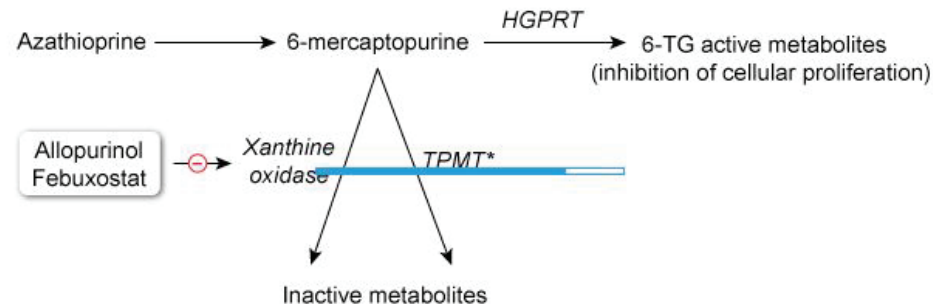
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Azathioprine metabolism



*Genetic deficiency of TPMT is common

6-TG = 6-thioguanine; HGPRT = hypoxanthine-guanine phosphoribosyltransferase;

TPMT = thiopurine methyltransferase

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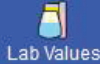
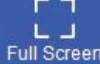
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that, like hypoxanthine and guanine, can follow 1 of 2 routes. Some 6-MP is converted by xanthine oxidase (or thiopurine methyltransferase) into inactive metabolites that are excreted in the urine. The remainder is converted by HGPRT into active metabolites (6-thioguanines), which act as false nucleotides that incorporate into DNA and RNA and inhibit hematopoietic cell proliferation. Therefore, when a **xanthine oxidase inhibitor is combined with azathioprine**, 6-MP is shunted toward **conversion into active metabolites**, leading to increased immunosuppression and risk of **cellular toxicity**.

(Choice B) Ganciclovir is similar in structure to guanosine and forms false purine nucleotides that disrupt DNA synthesis. It is relatively specific for viral DNA replication enzymes; it does not interact with allopurinol because it is not catabolized by xanthine oxidase.

(Choices C and D) Prednisone exerts a nonspecific immunosuppressive effect by inhibiting NF- κ B to regulate the transcription of leukoproliferative cytokines. Tacrolimus is a calcineurin inhibitor that suppresses T cells by preventing IL-2 transcription. Neither drug targets the purine degradation pathway and therefore is not significantly influenced by xanthine oxidase inhibition.

(Choice E) Trimethoprim inhibits dihydrofolate reductase to disrupt folate metabolism and inhibit the production of pyrimidine nucleotides. It is not affected by the inhibition of xanthine oxidase in the purine degradation pathway.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

because it is not catabolized by xanthine oxidase.

(Choices C and D) Prednisone exerts a nonspecific immunosuppressive effect by inhibiting NF- κ B to regulate the transcription of leukoproliferative cytokines. Tacrolimus is a calcineurin inhibitor that suppresses T cells by preventing IL-2 transcription. Neither drug targets the purine degradation pathway and therefore is not significantly influenced by xanthine oxidase inhibition.

(Choice E) Trimethoprim inhibits dihydrofolate reductase to disrupt folate metabolism and inhibit the production of pyrimidine nucleotides. It is not affected by the inhibition of xanthine oxidase in the purine degradation pathway.

Educational objective:

Azathioprine is an immunosuppression drug that is metabolized into active metabolites by HGPRT and, conversely, inactivated by xanthine oxidase. Coadministration with a xanthine oxidase inhibitor (eg, allopurinol, febuxostat) shunts azathioprine metabolism toward the production of active metabolites, resulting in increased immunosuppression and risk of cellular toxicity.

References

- [Myelosuppression associated with azathioprine-allopurinol interaction after heart and lung transplantation.](#)



1



Feedback



Suspend



End Block



A 3-year-old girl is brought to her pediatrician for a well child checkup. She has met all of the appropriate developmental milestones. Her height corresponds to the 60th percentile. Osteoblasts near the growth plates of her long bones secrete matrix material, and when they become trapped in the ossified matrix, they become known as osteocytes. These osteocytes remain connected to each other by:

- ☐ A. Tight junctions
- ☐ B. Hemidesmosomes
- ☐ C. Intermediate junctions
- ☐ D. Gap junctions
- ☐ E. Desmosomes


Submit



A 3-year-old girl is brought to her pediatrician for a well child checkup. She has met all of the appropriate developmental milestones. Her height corresponds to the 60th percentile. Osteoblasts near the growth plates of her long bones secrete matrix material, and when they become trapped in the ossified matrix, they become known as osteocytes. These osteocytes remain connected to each other by:

- ☐ A. Tight junctions (16%)
- ☐ B. Hemidesmosomes (5%)
- ☐ C. Intermediate junctions (14%)
- ☒ D. Gap junctions (46%)
- ☐ E. Desmosomes (16%)

Correct

 46%
Answered correctly 12 secs
Time Spent 09/20/2020
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Explanation

Block Time Remaining: 00:54:41

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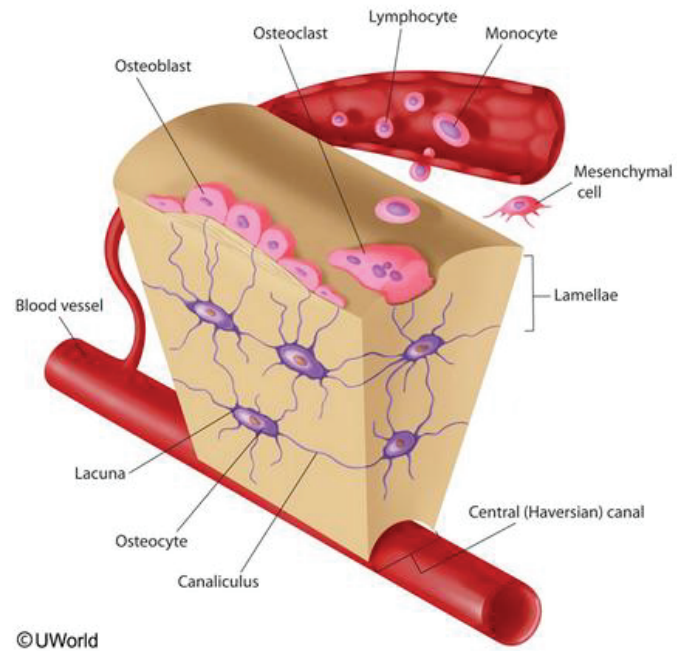
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Lymphocyte

Exhibit Display

Bone Structure: Osteocytes



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Within a single Haversian system, the central canal is encircled by multiple concentric lamellae of bony matrix that each contains lacunae filled with osteocytes and extracellular bone fluid. Delicate canaliculi radiate from each lacuna to create a reticular network with adjacent lacunae, and the cytoplasmic processes of the osteocytes lie within these canaliculi. These cytoplasmic processes send signals to and exchange nutrients and waste products with the osteocytes within neighboring lamellae via gap junctions.

The osteocytes serve to maintain the structure of the mineralized matrix and control the short-term release and deposition of calcium (i.e., calcium homeostasis). The plasma calcium concentration directly dictates the metabolic activity of osteocytes, while parathyroid hormone and calcitonin indirectly influence their metabolic activity. Osteocytes can also sense mechanical stresses and send signals to modulate the activity of surface osteoblasts, thereby helping to regulate bony remodeling.

(Choice A) Tight junctions (zonula occludens) are observed at the apices of glandular cells and consist of two closely adherent cytoplasmic membranes without an intervening space. Tight junctions are the first component of the junctional complex.

(Choice B) Hemidesmosomes are half desmosomes that extend from the basal surfaces of keratinocytes in the stratified squamous epithelium to attach to the basal lamina.



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice B) Hemidesmosomes are half desmosomes that extend from the basal surfaces of keratinocytes in the stratified squamous epithelium to attach to the basal lamina.

(Choice C) Intermediate junctions (zonula adherens) are a delicate network of cytoplasmic filaments that radiate from the cell membrane to hold adjacent cells together. Intermediate junctions are the second component of the junctional complex.

(Choice E) Desmosomes are small, circular, adherent patches circumferentially placed around cells that comprise the third component of the junctional complex. These patches are particularly common in stratified squamous epithelium and contribute significantly to the structural cohesiveness of tissues subject to mechanical stressors.

Educational objective:

Osteocytes have long intracanalicular processes that extend through the ossified bone matrix. These cytoplasmic processes send signals to and exchange nutrients and waste products with the osteocytes within neighboring lamellae via gap junctions. Osteocytes can sense mechanical stresses and send signals to modulate the activity of surface osteoblasts, thereby helping to regulate bony remodeling.

Histology

Rheumatology/Orthopedics & Sports

Bone remodeling



Feedback



Suspend



End Block



A 44-year-old woman comes to the office due to increasing right hip pain for the past several days. The pain is exacerbated by walking and by sitting with the right leg crossed over the left leg. The patient has a history of plantar fasciitis. Vital signs are within normal limits. BMI is 30 kg/m². On examination, right hip abduction and internal rotation against resistance when the hip is flexed reproduce the pain. The cause of this patient's symptoms is suspected to be pathology at a tendon insertion site. The tendon of which of the following muscles is most likely involved?

- ☐ A. Adductor brevis
- ☐ B. Gluteus medius
- ☐ C. Obturator externus
- ☐ D. Quadratus femoris
- ☐ E. Vastus lateralis

Submit

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A 44-year-old woman comes to the office due to increasing right hip pain for the past several days. The pain is exacerbated by walking and by sitting with the right leg crossed over the left leg. The patient has a history of plantar fasciitis. Vital signs are within normal limits. BMI is 30 kg/m². On examination, right hip abduction and internal rotation against resistance when the hip is flexed reproduce the pain. The cause of this patient's symptoms is suspected to be pathology at a tendon insertion site. The tendon of which of the following muscles is most likely involved?

- ☐ A. Adductor brevis (5%)
- ☒ B. Gluteus medius (52%)
- ☐ C. Obturator externus (23%)
- ☐ D. Quadratus femoris (7%)
- ☐ E. Vastus lateralis (10%)

Correct

52%
Answered correctly

02 mins, 02 secs
Time Spent

10/21/2020
Last Updated

Exhibit Display

Gluteal muscle attachments

Gluteus medius*Origin*

- Upper gluteal surface of the ilium

Insertion

- Greater trochanter of the femur

Gluteus minimus*Origin*

- Lower gluteal surface of the ilium

Insertion

- Greater trochanter of the femur

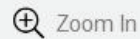
Gluteus maximus*Origin*

- Gluteal surface of the ilium, dorsal sacrum & coccyx, sacrotuberous ligament

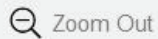
Insertion

- Gluteal tuberosity of the femur & the iliotibial tract

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Zoom In



Zoom Out



Reset



New

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3



Feedback



Suspend



End Block

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- 2
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This patient has **greater trochanteric pain syndrome (GTPS)** characterized by **lateral hip pain**. GTPS is an overuse tendinopathy of the **gluteus medius** and **gluteus minimus** at their insertion on the greater trochanter of the femur. It is often referred to as trochanteric bursitis, although bursal involvement varies and is not likely the primary pathology. Risk factors include obesity, plantar fasciitis, and altered gait mechanics (eg, osteoarthritis).

The gluteus medius and gluteus minimus originate from the upper and lower gluteal surfaces of the ilium, respectively, and insert onto the greater trochanter. Their primary functions include:

- **Hip abduction**
- Hip external rotation (internal rotation when the hip is flexed [eg, **leg crossing**])
- Horizontal stabilization of the pelvis during ambulation

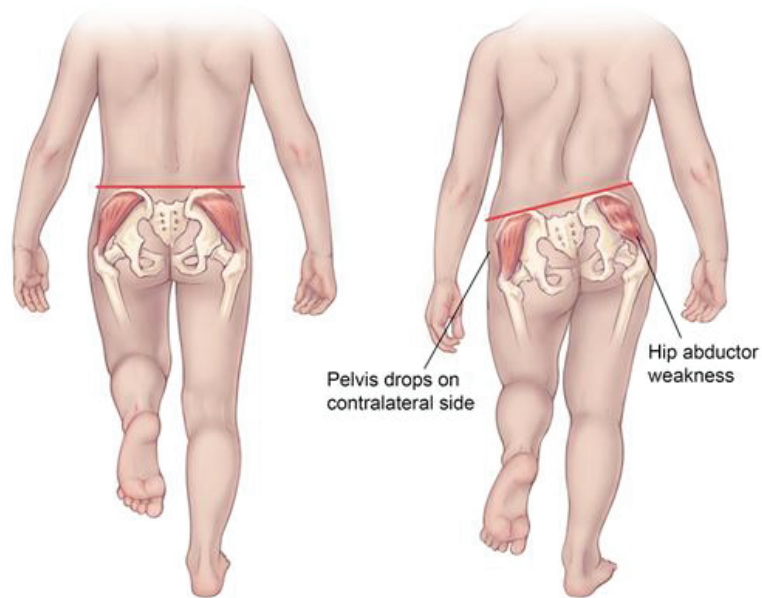
Examination typically is notable for **point tenderness** over the **greater trochanter**. The pain is reproduced by hip abduction and internal rotation (when the hip is flexed) against resistance because muscle contraction stresses the tendons. Sitting with the affected leg crossed over the other can also produce pain. Muscular weakness or tendon rupture is suggested by the **Trendelenburg sign**: with the patient standing on the affected leg, the pelvis falls to the contralateral side due to impaired abduction.

(Choice A) The **adductor brevis** originates from the inferior pubic ramus and inserts onto the linea aspera

This patient has **greater trochanteric pain syndrome (GTPS)** characterized by **lateral hip pain**. GTPS is

Exhibit Display

Trendelenburg sign



Normal

Abnormal

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Zoom Out

Reset

New | Existing

My Notebook

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- 2
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patient standing on the affected leg, the pelvis falls to the contralateral side due to impaired abduction.

(Choice A) The **adductor brevis** originates from the inferior pubic ramus and inserts onto the linea aspera of the femur. Strain typically produces groin and medial thigh pain that can be reproduced by resisted hip adduction (not abduction).

(Choices C and D) The **obturator externus** originates from the obturator membrane and obturator foramen and inserts onto the trochanteric fossa of the femur. The quadratus femoris originates from the ischial tuberosity and inserts onto the intertrochanteric crest of the femur. These muscles externally rotate the hip (regardless of whether the hip is flexed, unlike gluteus medius), and muscle strain would cause pain on resisted external (not internal) rotation.

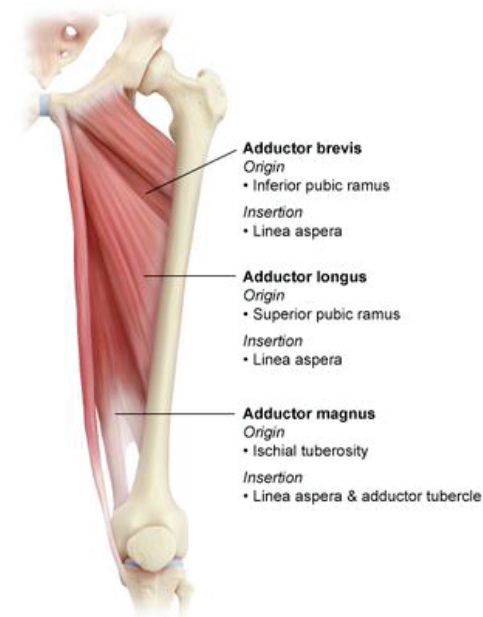
(Choice E) **Vastus lateralis** is part of the quadriceps femoris complex. It originates from the intertrochanteric line, greater trochanter, gluteal tuberosity, and linea aspera of the femur and inserts onto the tibial tubercle via the quadriceps tendon/patellar ligament. Strain presents with thigh pain that is reproduced by resisted knee extension.

Educational objective:

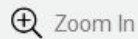
Greater trochanteric pain syndrome is an overuse tendinopathy of the gluteus medius and gluteus minimus at their insertion on the greater trochanter of the femur. Examination shows tenderness over the greater

Exhibit Display

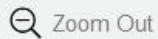
Muscular attachments of the major hip adductors



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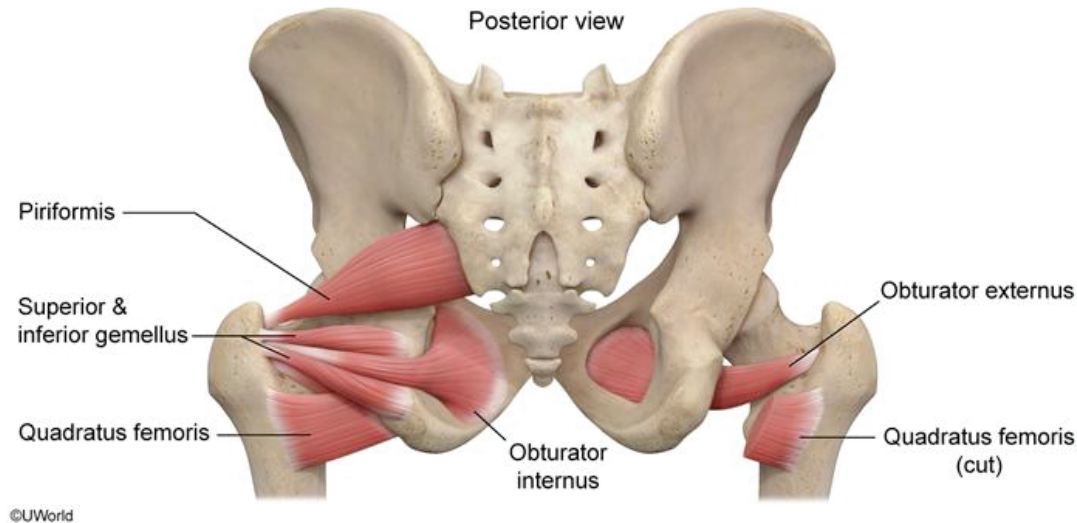
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Exhibit Display

Deep gluteal muscles

Posterior view



Zoom In

Zoom Out

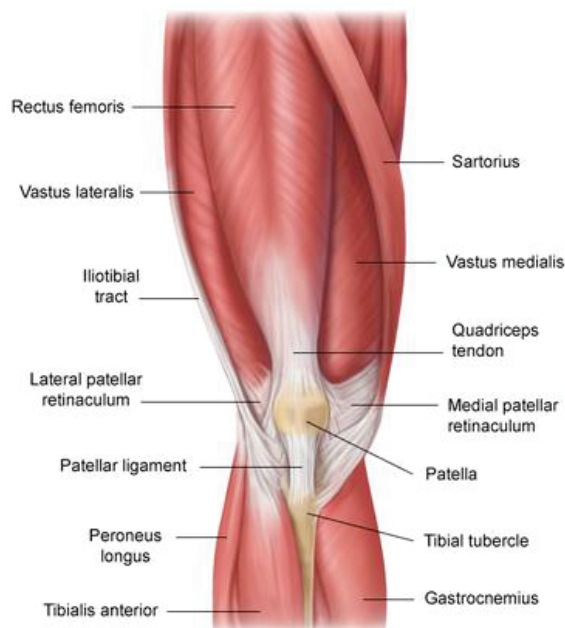
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My Notebook

Exhibit Display

Anterior knee anatomy



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Reset

New | Existing

My Notebook

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- 24
- 25
- 26
- 27

Item 1 of 40

Question Id: 20099

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice A) The **adductor brevis** originates from the inferior pubic ramus and inserts onto the linea aspera of the femur. Strain typically produces groin and medial thigh pain that can be reproduced by resisted hip adduction (not abduction).

(Choices C and D) The **obturator externus** originates from the obturator membrane and obturator foramen and inserts onto the trochanteric fossa of the femur. The quadratus femoris originates from the ischial tuberosity and inserts onto the intertrochanteric crest of the femur. These muscles externally rotate the hip (regardless of whether the hip is flexed, unlike gluteus medius), and muscle strain would cause pain on resisted external (not internal) rotation.

(Choice E) **Vastus lateralis** is part of the quadriceps femoris complex. It originates from the intertrochanteric line, greater trochanter, gluteal tuberosity, and linea aspera of the femur and inserts onto the tibial tubercle via the quadriceps tendon/patellar ligament. Strain presents with thigh pain that is reproduced by resisted knee extension.

Educational objective:

Greater trochanteric pain syndrome is an overuse tendinopathy of the gluteus medius and gluteus minimus at their insertion on the greater trochanter of the femur. Examination shows tenderness over the greater trochanter; pain is reproduced by resisted hip abduction and internal rotation (when the hip is flexed).

Block Time Remaining: 00:02:03

TUTOR

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3

Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 28-year-old man comes to the office with a 2-month history of dull low back pain and morning stiffness. The pain had an insidious onset, and the patient does not recall any recent trauma. He attempted treatment with acetaminophen and spinal manipulation, which did not provide relief. The patient has usually slept on his back but now must lie on his side to fall asleep easily. Past medical history is unremarkable. Vital signs are normal. Physical examination shows limited anterior flexion of the spine. There is no swelling or warmth of any peripheral joints. X-rays reveal narrowing of the sacroiliac joints. Which of the following is most strongly associated with this patient's disease?

- ☐ A. A specific human leukocyte antigen class I serotype
- ☐ B. A specific human leukocyte antigen class II serotype
- ☐ C. Auto-reactive immunoglobulin M antibodies
- ☐ D. Deficient complement component
- ☐ E. Selective immunoglobulin deficiency

Submit

Block Time Remaining: 00:02:04

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 28-year-old man comes to the office with a 2-month history of dull low back pain and morning stiffness. The pain had an insidious onset, and the patient does not recall any recent trauma. He attempted treatment with acetaminophen and spinal manipulation, which did not provide relief. The patient has usually slept on his back but now must lie on his side to fall asleep easily. Past medical history is unremarkable. Vital signs are normal. Physical examination shows limited anterior flexion of the spine. There is no swelling or warmth of any peripheral joints. X-rays reveal narrowing of the sacroiliac joints. Which of the following is most strongly associated with this patient's disease?

- ☒ A. A specific human leukocyte antigen class I serotype (61%)
- ☐ B. A specific human leukocyte antigen class II serotype (25%)
- ☐ C. Auto-reactive immunoglobulin M antibodies (11%)
- ☐ D. Deficient complement component (1%)
- ☐ E. Selective immunoglobulin deficiency (1%)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Ankylosing spondylitis is a chronic inflammatory disorder of the sacroiliac joints and axial skeleton. It is most common in young and middle-aged men and presents with morning stiffness and low back pain. Ankylosing spondylitis is characterized by destruction of articular cartilage with resulting stiffness and fusion of axial joints. The **sacroiliac joints** are often tender to palpation, and the spine may have decreased range of motion. X-ray of the sacroiliac joints may reveal erosions, sclerosis, narrowing, and ultimately **fusion** of the joint spaces. **Spine x-rays** reveal sclerosis, ligamentous calcification, and vertebral fusion ("bamboo spine").

Ankylosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease, and psoriatic arthritis are **seronegative spondyloarthropathies**, so-called due to the absence of serum rheumatoid factor. Patients with these diseases have a higher incidence of the **human leukocyte antigen (HLA) B27** allele compared to the general population, although most patients with HLA B27 will not develop spondyloarthropathies.

(Choice B) Class I HLA proteins (eg, HLA B27) are expressed by all nucleated cells and present endogenous antigens to CD8⁺ cytotoxic T cells. By contrast, HLA class II proteins (eg, DR, DP, DQ alleles) are expressed by antigen-presenting cells (eg, macrophages, dendritic cells) and present predominantly foreign antigens to CD4⁺ helper T cells. Conditions associated with HLA class II genotypes include



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Feedback



Suspend



End Block



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

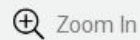
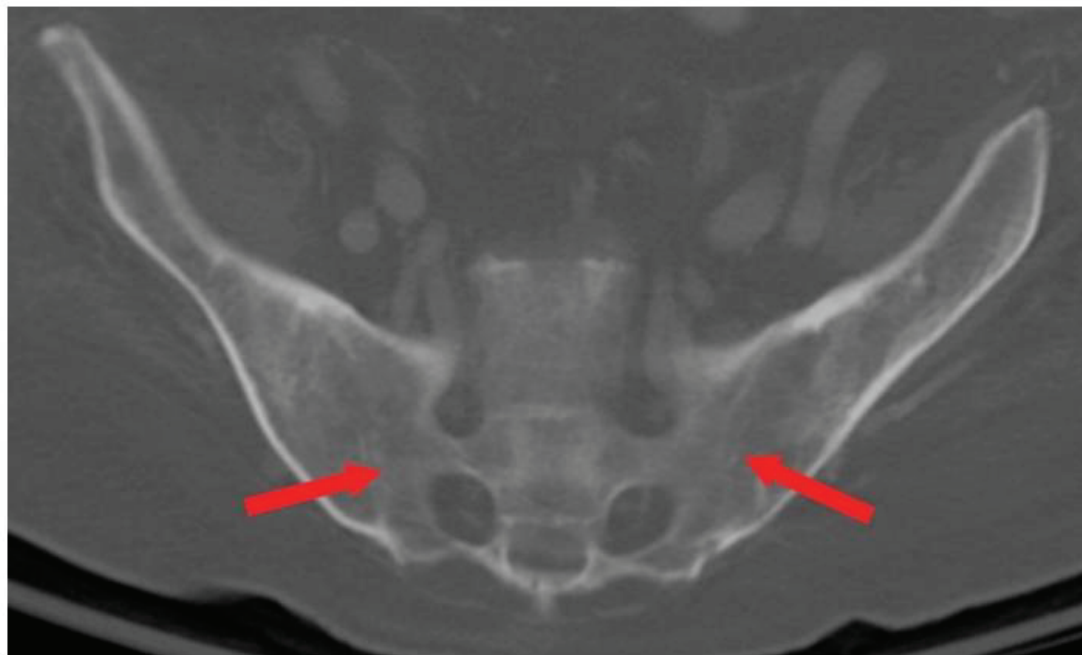


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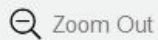


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Exhibit Display



Zoom In



Zoom Out



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My Notebook

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Feedback



Suspend



End Block

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21

22

23

24

25

26

27

Item 2 of 40

Question Id: 752

Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

foreign antigens to CD4+ helper T cells. Conditions associated with HLA class II genotypes include

Block Time Remaining: 00:03:02

TUTOR

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endogenous antigens to CD8⁺ cytotoxic T cells. By contrast, HLA class II proteins (eg, DR, DP, DQ alleles) are expressed by antigen-presenting cells (eg, macrophages, dendritic cells) and present predominantly foreign antigens to CD4⁺ helper T cells. Conditions associated with HLA class II genotypes include rheumatoid arthritis, type I diabetes mellitus, and celiac disease.

(Choice C) Rheumatoid factor (immunoglobulin [Ig] M antibodies against self IgG) is present in the majority of patients with rheumatoid arthritis and may be seen in a variety of other autoimmune diseases as well as in some healthy individuals.

(Choice D) Complement component deficiencies are associated with recurrent infections and systemic lupus erythematosus.

(Choice E) IgA deficiency causes recurrent mucosal and respiratory infections and anaphylactic reactions after the transfusion of blood products.

Educational objective:

The seronegative spondyloarthropathies include ankylosing spondylitis, reactive arthritis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease. Individuals expressing HLA B27 are at increased risk for the seronegative spondyloarthropathies.



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

An 18-year-old man, who was recently started on risperidone therapy for schizophrenia, comes to the office due to involuntary deviation of his head. On examination, the patient's head is tilted toward the right side and the chin is rotated to the left. There is palpable tightening of the right sternocleidomastoid muscle. It is determined that the patient is experiencing a medication-induced dystonic reaction due to motor neuron hyperactivity. The persistent myocyte stimulation causes a substance to be released from the sarcoplasmic reticulum. This substance most likely binds to which of the following proteins to cause this patient's symptoms?

- ☐ A. Actin
- ☐ B. Myosin
- ☐ C. Tropomyosin
- ☐ D. Troponin
- ☐ E. Protein kinase A

Submit

Block Time Remaining: 00:03:03

TUTOR

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1



Feedback



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End Block



An 18-year-old man, who was recently started on risperidone therapy for schizophrenia, comes to the office due to involuntary deviation of his head. On examination, the patient's head is tilted toward the right side and the chin is rotated to the left. There is palpable tightening of the right sternocleidomastoid muscle. It is determined that the patient is experiencing a medication-induced dystonic reaction due to motor neuron hyperactivity. The persistent myocyte stimulation causes a substance to be released from the sarcoplasmic reticulum. This substance most likely binds to which of the following proteins to cause this patient's symptoms?

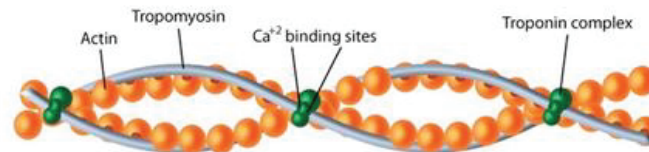
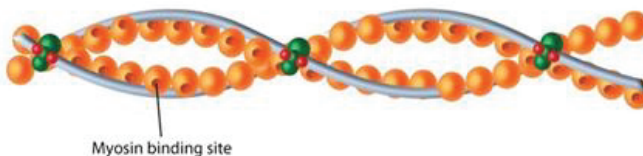
- ☐ A. Actin (2%)
- ☐ B. Myosin (4%)
- ☐ C. Tropomyosin (17%)
- ☒ D. Troponin (73%)
- ☐ E. Protein kinase A (1%)



Exhibit Display

 Ca^{+2} modulation of actin binding sites

Myosin binding sites blocked

Troponin- Ca^{+2} complex pulls tropomyosin away, exposing myosin binding sites

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Reset

New | Existing

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The **sarcoplasmic reticulum** (SR) is a modified endoplasmic reticulum within skeletal muscle cells. The SR forms a network of tubules with terminal cisterns that are in close contact with the T tubules (cytoplasmic membrane invaginations), allowing the membrane depolarization signal to reach the SR. The **Ca²⁺-ATPase pump** in the SR membrane actively sequesters calcium to keep intracellular concentrations low. Cell membrane depolarization causes **calcium release** from the SR into the cytoplasm via the SR **ryanodine receptor**.

Actin filaments, troponin complex (troponins C, T, and I), and tropomyosin form the thin filaments of muscle fibers. In the resting state, tropomyosin covers the **myosin binding sites** on the actin filaments. On release from the SR, **calcium** binds to troponin C on the thin filaments (**Choices A and C**). This induces a conformation change in the troponin complex, causing it to displace tropomyosin and expose the myosin binding sites on the actin filaments.

Myosin makes up the thick filaments of skeletal muscle. ATP is bound by the myosin head and cleaved to form ADP and inorganic phosphate ion, which are retained at the myosin head. When the myosin head binds to an actin filament, a conformational change causes the myosin to pull the actin filament, leading to muscle contraction and ADP release. A new ATP molecule then is bound to the myosin head, causing release of the actin filament. The cycle then repeats until calcium is displaced from troponin C and the



binds to an actin filament, a conformational change causes the myosin to pull the actin filament, leading to muscle contraction and ADP release. A new ATP molecule then is bound to the myosin head, causing release of the actin filament. The cycle then repeats until calcium is displaced from troponin C and the myosin binding sites are again covered (**Choice B**). The pulse of elevated intracellular calcium lasts only a fraction of a second before the calcium is resequenced within the SR.

(Choice E) Protein kinase A is activated by high intracellular concentrations of cAMP and is involved in the second messenger pathways of numerous hormones, including glucagon, beta adrenergic receptors, parathyroid hormone and others.

Educational objective:

During skeletal muscle contraction, calcium is released from the sarcoplasmic reticulum and binds troponin C, thereby allowing the binding of actin to myosin.

References

- [Troponin: regulatory function and disorders.](#)

Physiology

Subject

Rheumatology/Orthopedics & Sports

System

Muscle structure & physiology

Topic

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Block Time Remaining: 00:04:18

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1



Feedback



Suspend



End Block

A 34-year-old man with type 1 diabetes mellitus comes to the office due to achy pain in the shoulders, elbows, and thighs over the past several months. The patient was diagnosed with diabetes 15 years ago and has had difficulty adequately controlling it. He currently takes multiple daily injections of insulin. Vital signs are within normal limits. Physical examination shows mild pedal edema. Serum creatinine is 2.2 mg/dL, up from 1.6 mg/dL six months ago. Additional laboratory results show low serum calcium and elevated parathyroid hormone levels. Inhibition of which of the following enzymatic steps is most likely responsible for this patient's current symptoms?





Mark



Previous



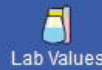
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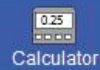
Tutorial



Lab Values



Notes



Calculator



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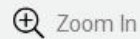
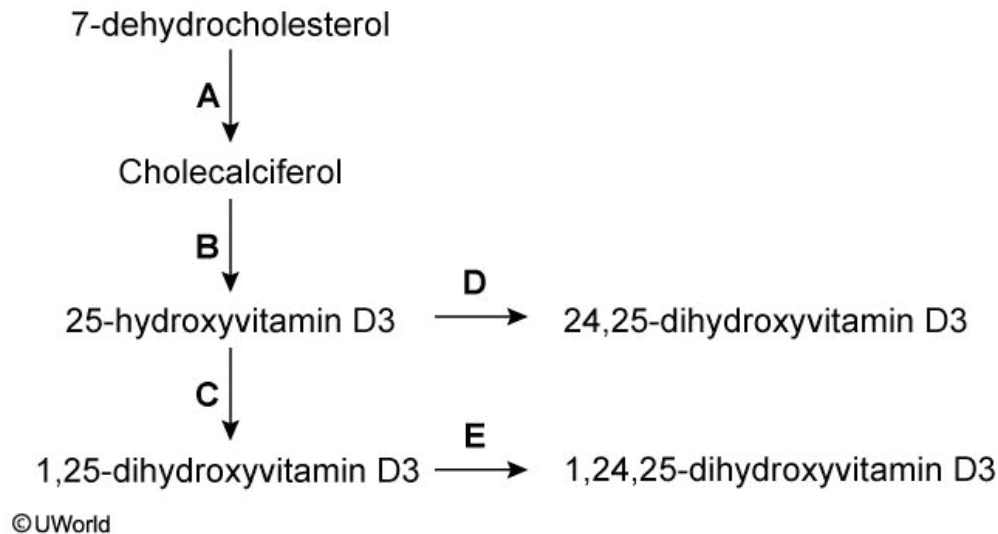


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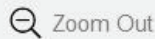


Settings

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



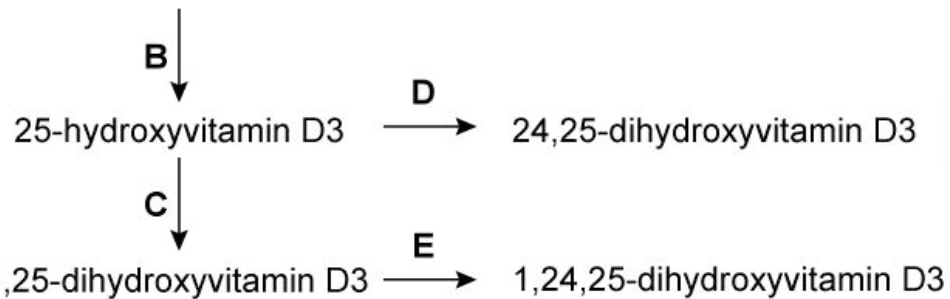
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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit

Block Time Remaining: 00:04:25

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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- ☐ A.A (1%)
- ☐ B.B (5%)
- ☒ C.C (82%)
- ☐ D.D (3%)
- ☐ E.E (6%)

Correct

82%



53 secs



10/09/2020

Block Time Remaining: 00:05:11

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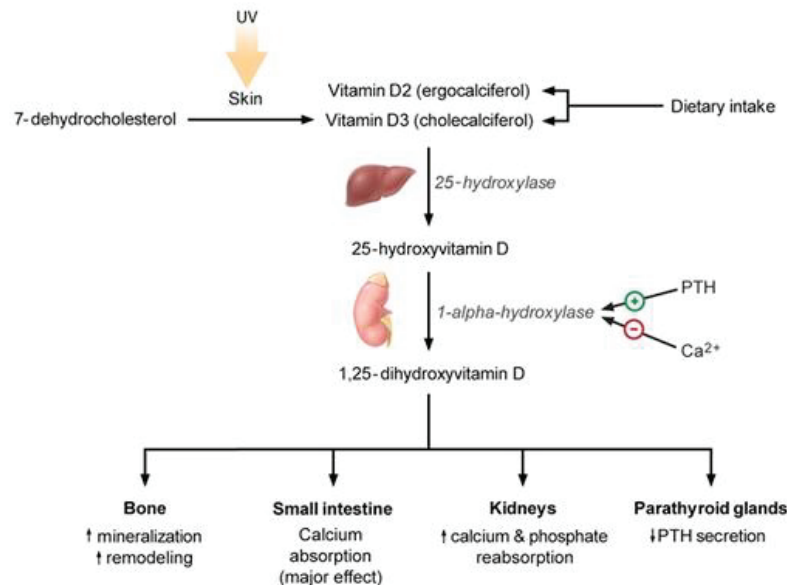
Feedback

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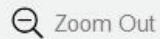
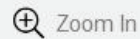
End Block

Exhibit Display

Normal vitamin D metabolism



PTH = parathyroid hormone.
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Synthesis of vitamin D begins in the skin with the conversion of 7-dehydrocholesterol to cholecalciferol (vitamin D₃) by ultraviolet light. Cholecalciferol is subsequently converted to 25-hydroxyvitamin D (the primary body store of vitamin D) by 25-hydroxylase in the liver. Finally, **25-hydroxyvitamin D** is filtered by renal glomeruli (with vitamin D-binding protein) and delivered to proximal tubule cells, where 1-alpha-hydroxylase converts it to **1,25-dihydroxyvitamin D**, the physiologically active form. The activity of 1-alpha-hydroxylase is upregulated by parathyroid hormone (PTH) and inhibited by fibroblast growth factor 23 (FGF23), a peptide secreted by osteocytes in response to high levels of 1,25-dihydroxyvitamin D.

Chronic kidney disease (CKD) results in impaired conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D due to the following factors:

- FGF23 levels increase early in CKD, causing direct inhibition of 1-alpha-hydroxylase
- Reduced glomerular filtration limits the delivery of 25-hydroxyvitamin D to proximal tubule cells
- Reduced functional renal mass limits production of 1-alpha-hydroxylase

Inadequate production of 1,25-dihydroxyvitamin D causes reduced intestinal absorption of calcium. This, along with increased phosphate retention (due to impaired glomerular and tubular function), leads to a compensatory increase in parathyroid hormone secretion (**secondary hyperparathyroidism**). Chronically increased PTH levels have a deleterious effect on bone metabolism (**renal osteodystrophy**), and can



increased PTH levels have a deleterious effect on bone metabolism (**renal osteodystrophy**), and can cause weakness, bone and muscle pain, defective bone mineralization, and an increased risk of fractures.

(Choice A) The initial step in vitamin D synthesis is driven by ultraviolet exposure in the skin. Factors that can lead to vitamin D deficiency include inadequate sunlight exposure (eg, institutionalized elders, living at extreme latitudes), use of high-grade sunblock, nocturnal occupations, and heavily pigmented skin.

(Choice B) 25-Hydroxyvitamin D deficiency due to inadequate 25-hydroxylase activity can be seen in patients with liver disease, but is uncommon and primarily seen in those with advanced cirrhosis.

(Choices D and E) Vitamin D-24-hydroxylase converts 25- and 1,25-dihydroxyvitamin D into inactive 24-hydroxylated metabolites; it functions to degrade excess levels of vitamin D. Although it is expressed predominantly in the kidneys and may be impaired in chronic kidney disease, loss of this enzyme would lead to higher 1,25-dihydroxyvitamin D levels and so would reduce, rather than worsen, the patient's symptoms.

Educational objective:

In chronic kidney disease, conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D is impaired. In addition, failure of glomerular and tubular function results in phosphate retention and hypocalcemia. This leads to a compensatory rise in parathyroid hormone (secondary hyperparathyroidism) that can present





extreme latitudes), use of high-grade sunblock, nocturnal occupations, and heavily pigmented skin.

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Educational objective:

In chronic kidney disease, conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D is impaired. In addition, failure of glomerular and tubular function results in phosphate retention and hypocalcemia. This leads to a compensatory rise in parathyroid hormone (secondary hyperparathyroidism) that can present with weakness, muscle and joint pain, defective bone mineralization, and increased fracture risk.

References

- [Impaired vitamin D metabolism in CKD.](#)



A 21-year-old man is brought to the emergency department following an assault. He was attempting to escape and turned away just as his attacker lunged toward him from behind with a knife. The patient suffered a 4-cm-wide penetrating injury with significant associated blood loss. Following initial stabilization, he is transferred to the operating room. Surgical exploration reveals injury to a muscle that assists in internal rotation of the arm and is innervated by the thoracodorsal nerve. Which of the following muscles depicted in the cadaveric specimen is most likely injured in this patient?

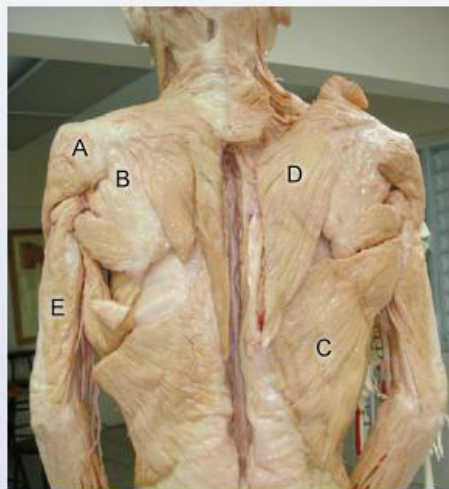
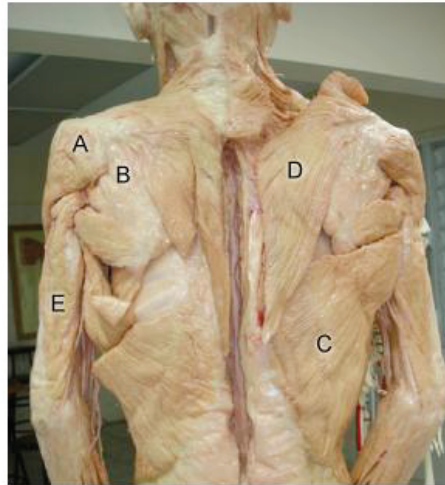


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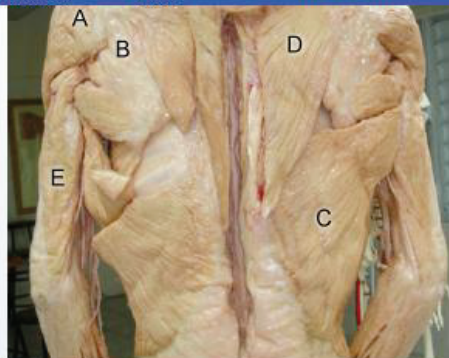
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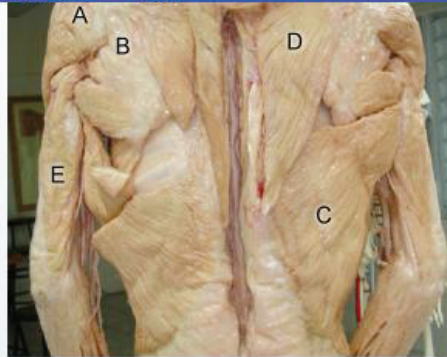
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My Notebook



- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit



- ☐ A.A (3%)
- ☐ B.B (20%)
- ☒ C.C (65%)
- ☐ D.D (8%)
- ☐ E.E (1%)

Correct

65%

49 secs

03/01/2021

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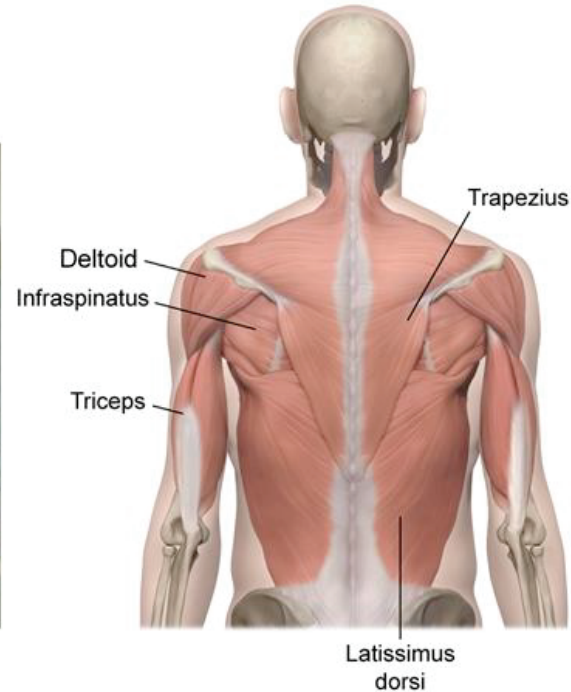
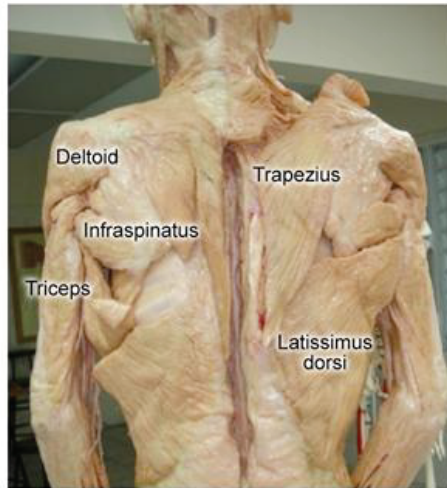
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Back and upper limb muscles



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The **latissimus dorsi** is a large thoracolumbar muscle that contributes to forceful movement of the humerus. It originates in a broad area spanning from the iliac crest and lumbar fascia to the spinous processes of T7-12 and lower ribs. It inserts at the bicipital groove of the humerus. The latissimus dorsi is innervated by the **thoracodorsal nerve**, with fibers originating from the C6-8 nerve roots. Primary functions include **extension, adduction, and internal rotation of the humerus**.

Due to its broad area and exposed location, the latissimus dorsi is vulnerable to injury from external trauma. It is also frequently injured in sports requiring forceful downward movement of the humerus, such as throwing, climbing, or swinging a tennis racket overhead.

(Choice A) The deltoid is innervated by the axillary nerve, and its primary action is abduction of the arm. It can be injured due to sudden or forceful loading of the arm while in abduction.

(Choice B) The infraspinatus is innervated by the suprascapular nerve and serves to externally rotate the arm. It is most commonly injured in association with the supraspinatus due to falls or overuse in older patients.

(Choice D) The trapezius is a large muscle in the upper back and neck that serves to elevate, rotate, and stabilize the scapula. It is primarily innervated by cranial nerve XI. The trapezius is frequently injured in rear-end (whiplash) motor vehicle accidents.

can be injured due to sudden or forceful loading of the arm while in abduction.

(Choice B) The infraspinatus is innervated by the suprascapular nerve and serves to externally rotate the arm. It is most commonly injured in association with the supraspinatus due to falls or overuse in older patients.

(Choice D) The trapezius is a large muscle in the upper back and neck that serves to elevate, rotate, and stabilize the scapula. It is primarily innervated by cranial nerve XI. The trapezius is frequently injured in rear-end (whiplash) motor vehicle accidents.

(Choice E) The triceps is innervated by the radial nerve (C6-8, T1) and is the primary muscle involved in extension of the elbow.

Educational objective:

The latissimus dorsi is a large thoracolumbar muscle that originates from the iliac crest and lumbar fascia to the spinous processes of T7-12 and lower ribs, and inserts at the bicipital groove of the humerus. It is innervated by the thoracodorsal nerve. Primary functions include extension, adduction, and medial (internal) rotation of the humerus.

Anatomy

Rheumatology/Orthopedics & Sports

Brachial plexus



A 45-year-old man comes to the emergency department due to 2 days of left knee swelling and pain. The patient has no significant past medical history apart from an episode of facial palsy 3 months ago. Six months ago, he went on a hiking trip to New Hampshire but has no other travel history. The patient is in a long-standing monogamous relationship with his wife and has had no other sexual partners. Temperature is 37.1 C (98.8 F). Examination shows left knee joint swelling with no surrounding erythema. The remainder of the musculoskeletal examination is unremarkable. There is no heart murmur. Which of the following might have prevented this patient's knee condition?

- ☐ A. Allopurinol
- ☐ B. Ceftriaxone
- ☐ C. Lamivudine
- ☐ D. Live attenuated vaccine
- ☐ E. Mefloquine
- ☐ F. Metronidazole



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- ☐ A. Allopurinol (10%)
- ☒ B. Ceftriaxone (65%)
- ☐ C. Lamivudine (2%)
- ☐ D. Live attenuated vaccine (6%)
- ☐ E. Mefloquine (6%)
- ☐ F. Metronidazole (7%)

Correct

65%

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10/20/2020

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- ☐ D. Live attenuated vaccine (6%)
- ☐ E. Mefloquine (6%)
- ☐ F. Metronidazole (7%)

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Last Updated

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This patient has symptoms consistent with long-standing **Lyme disease**. Lyme disease is caused by the spirochete ***Borrelia burgdorferi***, which is transmitted by the bite of an *Ixodes* tick. Lyme disease is endemic in the northeastern United States and northern Europe. Like syphilis, another spirochetal infection, Lyme disease progresses through a predictable series of phases:

1. Early localized phase: Days to weeks following exposure, patients experience flu-like symptoms and the characteristic cutaneous eruption, **erythema chronicum migrans (ECM)**.
2. Early disseminated phase: Weeks or months later, there may be central nervous system (eg, **facial palsy**) and/or cardiac involvement (eg, atrioventricular **nodal block**).
3. Late Lyme disease: This phase, which occurs months to years post-exposure, is rare given the frequency with which patients receive antibiotics for other indications. Patients may experience **asymmetric arthritis** (most often involving a **single knee joint**, as in this patient) and/or subacute **encephalopathy** with decreased memory, somnolence, and mood changes.

Lyme disease is easily treated with **doxycycline** or penicillin-type antibiotics (eg, ceftriaxone). This patient does not appear to have noted ECM, for which he would likely have received doxycycline. However, treatment with **ceftriaxone** when he developed the facial palsy (a possible manifestation of early disseminated Lyme disease) would have prevented progression to late Lyme disease.



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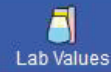
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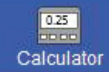
Tutorial



Lab Values



Notes



Calculator



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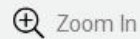


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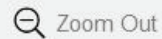


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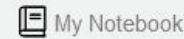
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My Notebook



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Feedback



Suspend



End Block



disseminated Lyme disease) would have prevented progression to late Lyme disease.

(Choice A) Allopurinol competitively inhibits xanthine oxidase, suppressing uric acid synthesis. This drug is used to treat gout and prevent uric acid kidney stones and tumor lysis syndrome.

(Choice C) Lamivudine is a nucleoside reverse transcriptase inhibitor used for HIV treatment.

(Choice D) A *Borrelia burgdorferi* vaccine, now discontinued due to low sales, contains a recombinant outer surface protein from these bacteria, not live organisms.

(Choice E) Mefloquine is an antimalarial drug used in prevention and treatment of *Plasmodium falciparum* infections, among others.

(Choice F) Metronidazole is effective against anaerobic bacteria (eg, *Clostridium difficile*, *Bacteroides*) and parasites (eg, *Entamoeba histolytica*, *Giardia lamblia*, *Trichomonas vaginalis*).

Educational objective:

Early Lyme disease causes flu-like symptoms and erythema chronicum migrans. The second stage of Lyme disease may involve atrioventricular block and facial palsy. Late Lyme disease can cause chronic asymmetric large joint arthritis and encephalopathy. Lyme disease is easily treated with doxycycline or penicillin-type antibiotics (eg, ceftriaxone).



A 66-year-old postmenopausal woman comes to the office to discuss her bone densitometry results. She has a history of hypertension and has smoked a pack of cigarettes daily for 30 years. BMI is 20.1 kg/m². Physical examination is unremarkable. Bone densitometry reveals low bone density consistent with osteoporosis. The patient is prescribed risedronate. Repeat bone densitometry 2 years later reveals no further loss of bone mineral density. Which of the following mechanisms most likely explains the drug's effect on bone mineral density?

- ☐ A. Decreased osteocyte-mediated inhibition of bone formation
- ☐ B. Decreased stimulation of receptor activator of nuclear factor kappa-B
- ☐ C. Decreased urinary calcium excretion
- ☐ D. Increased intestinal calcium absorption
- ☐ E. Inhibition of osteoclast-mediated bone resorption
- ☐ F. Stimulation of preosteoblasts to mature osteoblasts

Submit

A 66-year-old postmenopausal woman comes to the office to discuss her bone densitometry results. She has a history of hypertension and has smoked a pack of cigarettes daily for 30 years. BMI is 20.1 kg/m². Physical examination is unremarkable. Bone densitometry reveals low bone density consistent with osteoporosis. The patient is prescribed **risedronate**. Repeat bone densitometry 2 years later reveals no further loss of bone mineral density. Which of the following mechanisms most likely explains the drug's effect on bone mineral density?

- ☐ A. ~~Decreased osteocyte-mediated inhibition of bone formation~~ (1%)
- ☐ B. Decreased stimulation of receptor activator of nuclear factor kappa-B (7%)
- ☐ C. ~~Decreased urinary calcium excretion~~ (0%)
- ☐ D. ~~Increased intestinal calcium absorption~~ (1%)
- ☒ E. Inhibition of osteoclast-mediated bone resorption (87%)
- ☐ F. Stimulation of preosteoblasts to mature osteoblasts (1%)

Medications for osteoporosis

| | |
|--|--|
| Calcium & vitamin D | <ul style="list-style-type: none">• Given as needed to ensure adequate intake |
| Bisphosphonates (eg, alendronate, risedronate) | <ul style="list-style-type: none">• Attach to hydroxyapatite binding sites on bone surfaces• Inhibit osteoclast-mediated bone resorption |
| Denosumab | <ul style="list-style-type: none">• Binds RANK-L & inhibits binding to RANK• Reduces differentiation & survival of osteoclasts |
| Recombinant PTH analog (teriparatide) | <ul style="list-style-type: none">• Stimulates maturation of preosteoblasts into bone-forming osteoblasts• Increases gastrointestinal calcium absorption & renal tubular calcium reabsorption |

RANK = receptor activator of nuclear factor kappa-B; **RANK-L** = RANK ligand; **PTH** = parathyroid hormone.

Bisphosphonates (eg, alendronate, risedronate) treat osteoporosis by **inhibiting osteoclast-mediated bone resorption**. They have a chemical structure similar to that of pyrophosphate and attach to

Bisphosphonates (eg, alendronate, risedronate) treat osteoporosis by **inhibiting osteoclast-mediated bone resorption**. They have a chemical structure similar to that of pyrophosphate and attach to hydroxyapatite binding sites on bony surfaces. Osteoclasts that resorb the bone take up the bisphosphonate and are unable to adhere to the bony surface to continue resorption. Bisphosphonates also decrease osteoclast proton production, induce osteoclast apoptosis, and decrease development/recruitment of osteoclast precursor cells. The net result is to **slow the rate of bone loss**, and some patients may experience a small increase in bone mineral density.

(Choice A) Sclerostin is a glycoprotein produced by osteocytes that inhibits osteoblast bone formation. Monoclonal antibody preparations (eg, romosozumab) that bind sclerostin reverse this effect and facilitate increased osteoblast activity.

(Choice B) Denosumab is a monoclonal antibody that decreases bone resorption by binding to the receptor activator of nuclear factor kappa-B ligand (RANK-L) and blocking the interaction between RANK-L and RANK (a receptor located on osteoclast surfaces), which is required for preosteoclast maturation to osteoclasts.

(Choices C, D, and F) Teriparatide is a recombinant formulation identical to the 34-amino-acid sequence at the N-terminal portion of endogenous parathyroid hormone (PTH). Similar to PTH, teriparatide

(Choice B) Denosumab is a monoclonal antibody that decreases bone resorption by binding to the receptor activator of nuclear factor kappa-B ligand (RANK-L) and blocking the interaction between RANK-L and RANK (a receptor located on osteoclast surfaces), which is required for preosteoclast maturation to osteoclasts.

(Choices C, D, and F) Teriparatide is a recombinant formulation identical to the 34-amino-acid sequence at the N-terminal portion of endogenous parathyroid hormone (PTH). Similar to PTH, teriparatide stimulates maturation of preosteoblasts into bone-forming osteoblasts that lay down collagen and eventually mineralize the matrix. Teriparatide also increases gastrointestinal calcium absorption and renal tubular calcium reabsorption, which leads to decreased urinary calcium excretion.

Educational objective:

Bisphosphonates have a chemical structure similar to that of pyrophosphate and attach to hydroxyapatite binding sites on bony surfaces to inhibit bone resorption by osteoclasts.

Pharmacology
Subject

Rheumatology/Orthopedics & Sports
System

Osteoporosis
Topic

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A 2-year-old boy is brought to the emergency department due to high fever and malaise for the past 4 days. His parents say that he began limping yesterday and now refuses to walk. The patient has had no recent travel or exposure to anyone with similar symptoms. Temperature is 39.4 C (103 F). Passive range of motion of the hips, knees, and ankles does not elicit pain. There are no joint effusions. The patient refuses to bear weight. An intravenous radiotracer that localizes to areas of increased osteoblastic activity is administered, and several images are obtained to find areas with atypical activity. Abnormally increased uptake of the radiotracer is most likely to be seen in which of the following areas?

- ☐ A. Flat bone
- ☐ B. Long bone diaphysis
- ☐ C. Long bone epiphysis
- ☐ D. Long bone metaphysis
- ☐ E. Vertebral body

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Next



Full Screen



Tutorial



Lab Values



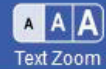
Notes



Calculator



Reverse Color



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- ☐ A. Flat bone (1%)
- ☐ B. Long bone diaphysis (25%)
- ☒ C. Long bone epiphysis (25%)
- ☐ D. Long bone metaphysis (44%)
- ☐ E. Vertebral body (2%)

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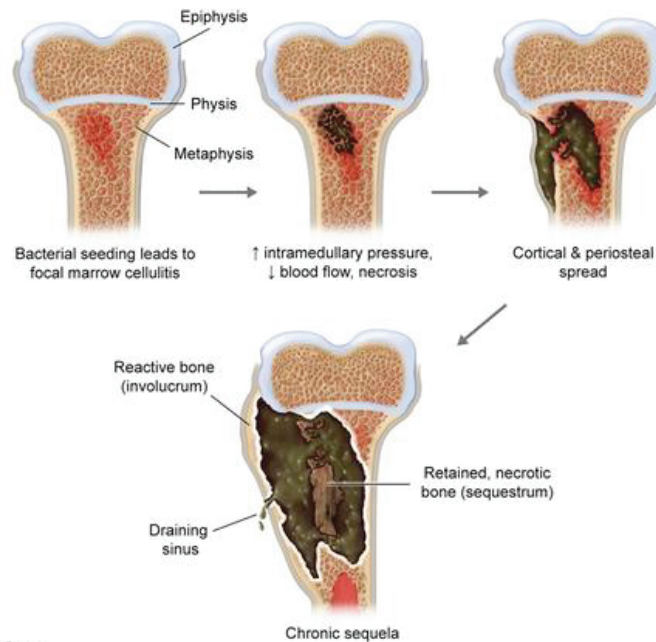
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Progression of hematogenous osteomyelitis



Zoom In

Zoom Out

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My Notebook



This child has acute-onset **fever**, malaise, and **refusal to bear weight**, findings concerning for **osteomyelitis**. Older children often have focal bony tenderness, but children age ≤ 2 may be unable to localize pain. Passive range of motion of the joints typically is normal and helps distinguish osteomyelitis from septic arthritis.

The most common cause of osteomyelitis in **children** is **hematogenous spread** of bacteria, which may be introduced by minor (often unnoticed) trauma to a distant site. Infection in children classically occurs in the **metaphyses of long bones** (eg, femur, tibia) because this region is highly vascular yet contains **slow-flowing sinusoids** that are conducive to bacterial seeding. Bacterial seeding within the metaphysis initially causes **acute inflammation** of the bone marrow, with focal hyperperfusion and **increased radiotracer uptake** within the affected region.

Persistent inflammation within the confined bony space leads to increased intramedullary pressure, which compromises blood flow and forces infectious exudate into the cortex and periosteum. Without treatment, the infection can progress to chronic suppurative osteomyelitis, in which necrotic bone (ie, sequestrum) serves as an infectious reservoir and sinus tracts develop to drain away the purulent material.

(Choice A) Osteomyelitis of flat bones (eg, skull, pelvis) is uncommon in children and is typically caused





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

serves as an infectious reservoir and sinus tracts develop to drain away the purulent material.

(Choice A) Osteomyelitis of flat bones (eg, skull, pelvis) is uncommon in children and is typically caused by contiguous spread of infection (eg, open wound, dental abscess). Although pelvic bone involvement may lead to refusal to bear weight, this patient has no gross abnormality of the hips or lower extremities suggesting adjacent soft tissue infection.

(Choice B) Ewing sarcoma typically arises in diaphysis of the long bones, especially the femur. It is the second most common malignant bone tumor in children after osteosarcoma. However, Ewing sarcoma typically presents in children age >10 with an insidious onset of progressive pain, not in toddlers with acute refusal to bear weight.

(Choice C) The physis (growth plate) in children limits vascular connections between the metaphysis and epiphysis, which is relatively less vascularized, making epiphyseal involvement uncommon in hematogenous osteomyelitis. Although avascular necrosis of the proximal femoral epiphysis (eg, Legg-Calve-Perthes) can present with a limp, the pain is typically more mild and develops gradually without fever.

(Choice E) Hematogenous osteomyelitis in adults occurs more commonly in the vertebral bodies due to increasing vertebral vascularity with age as well as epiphyseal closure during puberty (improves capillary



1



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(Choice E) Hematogenous osteomyelitis in adults occurs more commonly in the vertebral bodies due to increasing vertebral vascularity with age as well as epiphyseal closure during puberty (improves capillary flow within the metaphyses of long bones).

Educational objective:

Hematogenous osteomyelitis occurs most commonly in children. It usually affects the metaphysis of long bones due to the presence of slow-flowing sinusoids that are conducive to bacterial seeding. Fever and refusal to bear weight are common manifestations in young children who are unable to localize the pain.

References

- [Hematogenous osteomyelitis in infants and children: imaging of a changing disease.](#)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 53-year-old man comes to the office with a dull ache in his right shoulder. The pain is worse with movement and often interferes with his sleep. The patient cannot recall any traumatic events prior to the start of the pain but did experience increased discomfort after helping his daughter move into her college dorm room a week ago. His past medical history includes dyslipidemia and hypertension, for which he takes the appropriate medications. Physical examination reveals localized tenderness just below the acromion. The physician asks the patient to abduct his arms 90 degrees to the side and flex them 30 degrees forward with his thumbs pointing to the floor. She then applies downward force to his arms. This maneuver elicits pain in the patient's right shoulder and reveals right-sided weakness as compared to the left side. A tendon of which of the following muscles is most likely injured in this patient?

- ☐ A. Biceps brachii
- ☐ B. Deltoid
- ☐ C. Levator scapulae
- ☐ D. Serratus anterior
- ☐ E. Supraspinatus



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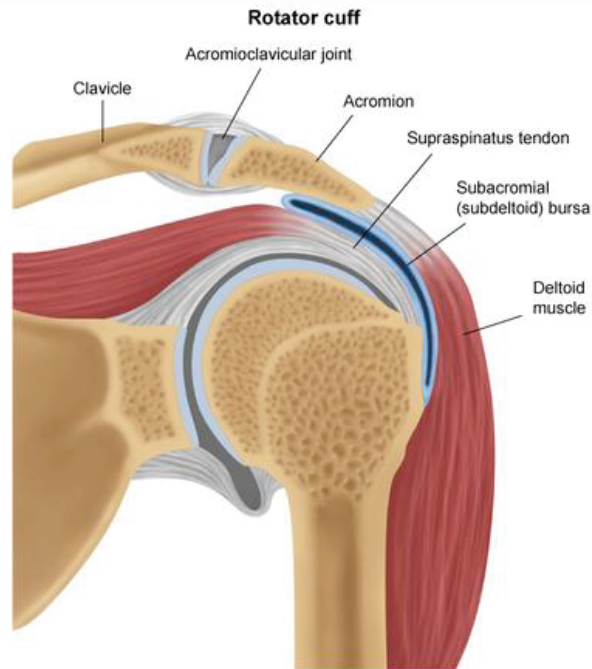


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movement and often interferes with his sleep. The patient cannot recall any traumatic events prior to the start of the pain but did experience increased discomfort after helping his daughter move into her college dorm room a week ago. His past medical history includes dyslipidemia and hypertension, for which he takes the appropriate medications. Physical examination reveals localized tenderness just below the **acromion**. The physician asks the patient to abduct his arms 90 degrees to the side and flex them 30 degrees forward with his thumbs pointing to the floor. She then applies downward force to his arms. This maneuver elicits pain in the patient's right shoulder and reveals right-sided weakness as compared to the left side. A tendon of which of the following muscles is most likely injured in this patient?

- ☐ A. Biceps brachii (5%)
- ☐ B. Deltoid (17%)
- ☐ C. Levator scapulae (3%)
- ☐ D. Serratus anterior (2%)
- ☒ E. Supraspinatus (69%)

Exhibit Display



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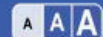
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The **rotator cuff** consists of the tendons of the **supraspinatus**, **infraspinatus**, **teres** minor, and **subscapularis (SITS)** and contributes to the stability and motion of the glenohumeral joint. During abduction of the humerus, the supraspinatus initiates movement through the first 10-15 degrees; subsequently, the deltoid provides the primary abductive force while the supraspinatus provides stability to the joint.

Of all the rotator cuff structures, the **supraspinatus tendon** is most commonly affected in rotator cuff syndrome. This tendon is vulnerable to chronic repeated trauma from **impingement** between the head of the humerus and the acromion during abduction. Inflammation and fibrosis can worsen the problem by increasing friction between the head of the humerus and the acromion, as well as causing inflammation of the subacromial bursa. On examination, the action of the supraspinatus can be isolated with the "empty-can" supraspinatus test: abduction of the humerus in parallel to the axis of the scapula (30 degrees forward flexion) while in full internal rotation (thumbs pointed to the floor).

(Choice A) The long head of the biceps brachii originates on the supraglenoid tubercle of the scapula and inserts on the radius. It primarily flexes and supinates the forearm, although it also contributes to shoulder flexion. Biceps tendonitis is characterized by tenderness at the bicipital groove (separates lesser and



(Choice A) The long head of the biceps brachii originates on the supraglenoid tubercle of the scapula and inserts on the radius. It primarily flexes and supinates the forearm, although it also contributes to shoulder flexion. Biceps tendonitis is characterized by tenderness at the bicipital groove (separates lesser and greater tubercles of the humerus).

(Choice B) The deltoid originates on the clavicle, the acromion, and the spine of the scapula; it inserts on the lateral humerus. Deltoid injuries are less common than supraspinatus injuries and usually manifest as sudden-onset shoulder pain after overloading the arm while in abduction.

(Choice C) The tendons of the levator scapulae insert on the superomedial border of the scapula and on the transverse processes of the C1 through C4 vertebrae. The levator scapulae does not contribute to the stability of the glenohumeral joint.

(Choice D) The serratus anterior originates on the lateral surfaces of the first 8 ribs and inserts on the scapula. Its primary action is to pull the scapula forward and rotate it to raise the glenoid. Injury to the long thoracic nerve causes paralysis of this muscle and "winging" of the scapula.

Educational objective:

The supraspinatus muscle assists in abduction of the arm and stabilization of the glenohumeral joint. The supraspinatus tendon is vulnerable to injury due to impingement between the acromion and the head of the



(Choice B) The deltoid originates on the clavicle, the acromion, and the spine of the scapula; it inserts on the lateral humerus. Deltoid injuries are less common than supraspinatus injuries and usually manifest as sudden-onset shoulder pain after overloading the arm while in abduction.

(Choice C) The tendons of the levator scapulae insert on the superomedial border of the scapula and on the transverse processes of the C1 through C4 vertebrae. The levator scapulae does not contribute to the stability of the glenohumeral joint.

(Choice D) The serratus anterior originates on the lateral surfaces of the first 8 ribs and inserts on the scapula. Its primary action is to pull the scapula forward and rotate it to raise the glenoid. Injury to the long thoracic nerve causes paralysis of this muscle and "winging" of the scapula.

Educational objective:

The supraspinatus muscle assists in abduction of the arm and stabilization of the glenohumeral joint. The supraspinatus tendon is vulnerable to injury due to impingement between the acromion and the head of the humerus. Supraspinatus tendinopathy is the most common cause of rotator cuff syndrome.

References

- [Chronic shoulder pain: part I. Evaluation and diagnosis.](#)



A 58-year-old woman comes to the office with left knee pain. The pain began a year ago and has progressively become more severe. The pain is worse later in the day and is now limiting her normal day-to-day activities. She has no history of injury to the joint and has no significant pain in any other joints. The patient has attempted treatment with acetaminophen, but that has not provided adequate relief. She does not use tobacco, alcohol, or illicit drugs and works as a school bus driver. Her BMI is 34 kg/m². Left knee joint examination shows a mild effusion, crepitus on movement, and joint line tenderness. The patient is started on celecoxib therapy. The presence of which of the following conditions in this patient's medical history would make this medication the preferred treatment?

- ☐ A. Hyperlipidemia
- ☐ B. Hypertension
- ☐ C. Peptic ulcer disease
- ☐ D. Renal impairment
- ☐ E. Stable angina

progressively become more severe. The pain is worse later in the day and is now limiting her normal day-to-day activities. She has no history of injury to the joint and has no significant pain in any other joints. The patient has attempted treatment with acetaminophen, but that has not provided adequate relief. She does not use tobacco, alcohol, or illicit drugs and works as a school bus driver. Her BMI is 34 kg/m². Left knee joint examination shows a mild effusion, crepitus on movement, and joint line tenderness. The patient is started on celecoxib therapy. The presence of which of the following conditions in this patient's medical history would make this medication the preferred treatment?

- ☐ A. Hyperlipidemia (3%)
- ☐ B. Hypertension (1%)
- ☒ C. Peptic ulcer disease (83%)
- ☐ D. Renal impairment (7%)
- ☐ E. Stable angina (3%)

Correct

83%

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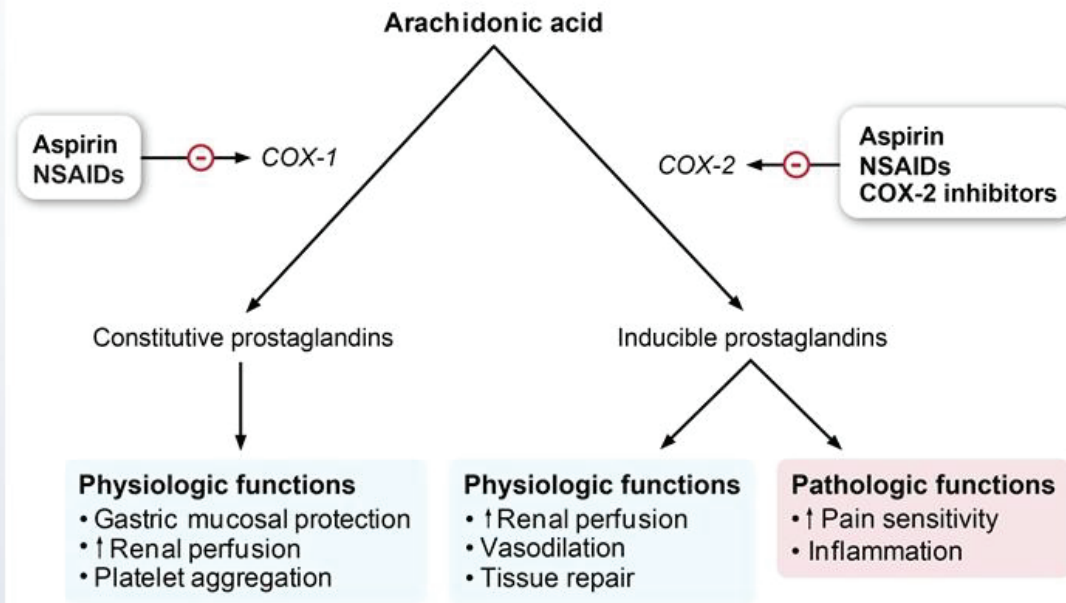
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Cyclooxygenase inhibitors



COX: cyclooxygenase, NSAIDs: nonsteroidal anti-inflammatory drugs

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Cyclooxygenase (COX; prostaglandin synthase) initiates the synthesis of prostanoids (eg, prostaglandins, thromboxane) from **arachidonic acid**. COX exists in 2 primary forms:



COX: cyclooxygenase, NSAIDs: nonsteroidal anti-inflammatory drugs

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Cyclooxygenase (COX; prostaglandin synthase) initiates the synthesis of prostanoids (eg, prostaglandins, thromboxane) from **arachidonic acid**. COX exists in 2 primary forms:

- COX 1, which plays a physiologic role in a number of normally functioning tissues (eg, platelets, gastrointestinal tract)
- COX 2, which is preferentially expressed at sites of inflammation.

Nonsteroidal anti-inflammatory drugs (NSAIDs) work by inhibiting COX to block prostaglandin synthesis. Most NSAIDs inhibit both the COX 1 and COX 2 isoenzymes. However, inhibition of COX 1 may lead to severe adverse effects, including **gastric ulceration** (reduced mucosal protection) and **increased bleeding** (decreased platelet aggregation). Selective **COX 2 inhibitors** (eg, celecoxib) have potent anti-inflammatory effects with **less risk** of bleeding and gastrointestinal ulceration. They are recommended for use in patients at risk for gastrointestinal complications, such as those with prior peptic ulcer disease. The risk for ulcers can also be reduced by combining a nonselective NSAID with a second drug (eg, proton pump inhibitors, misoprostol) to reduce gastric acid secretion.

(Choice A) Selective COX 2 inhibitors do not have a substantial effect on serum lipids.

(Choices B and D) Both COX 1 and COX 2 are expressed in renal tissues. Therapy with either

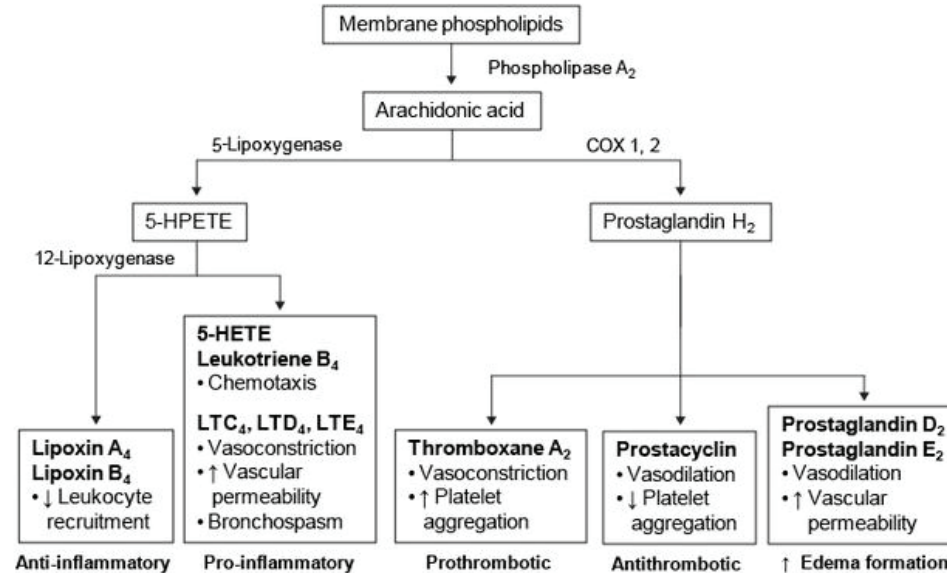


COX: cyclooxygenase NSAIDs: nonsteroidal anti-inflammatory drugs

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Arachidonic acid metabolic pathways



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(Choice A) Selective COX 2 inhibitors do not have a substantial effect on serum lipids.

(Choices B and D) Both COX 1 and COX 2 are expressed in renal tissues. Therapy with either nonselective NSAIDs or selective COX 2 inhibitors can cause fluid retention, aggravation of hypertension, and impaired renal function.

(Choice E) COX 2 is expressed in vascular endothelial cells and vascular smooth muscle cells, where it plays a role in the local production of **prostacyclin**, which has anticoagulant and vasodilatory actions. COX 2 inhibitors have been associated with an increased risk of cardiovascular events.

Educational objective:

Selective cyclooxygenase 2 (COX 2) inhibitors relieve pain with lower risk of bleeding and gastric ulceration than nonselective nonsteroidal anti-inflammatory drugs.

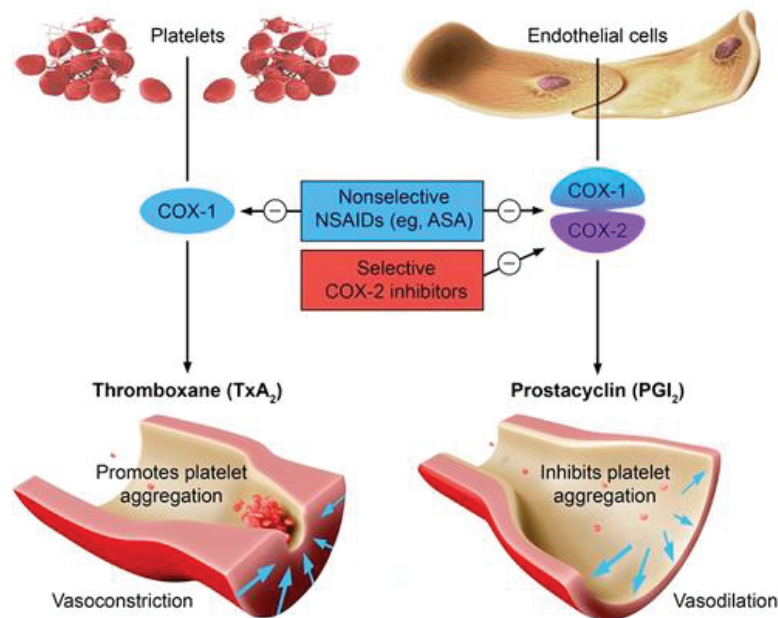
References

- [Comparison of gastrointestinal adverse effects between cyclooxygenase-2 inhibitors and non-selective, non-steroidal anti-inflammatory drugs plus proton pump inhibitors: a systematic review and meta-analysis.](#)

Pharmacology Rheumatology/Orthopedics & Sports Cox 2 inhibitor

Exhibit Display

Effects of COX inhibition on platelets & endothelial cells



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A 13-year-old boy is brought to the office due to right knee pain. Several weeks ago, he developed mild anterior knee pain that has gradually worsened and now causes him to limp. The pain has significantly limited his participation in basketball practice. It is relieved by rest and can be reproduced when the patient straightens out his right knee while seated in a chair. Further evaluation reveals an avulsion fracture affecting a developing secondary ossification center due to muscle overuse. Which of the following structures is most likely involved in this patient's disease process?

- ☐ A. Anterior intercondylar area
- ☐ B. Anteromedial tibia shaft
- ☐ C. Fibular head
- ☐ D. Medial condyle of tibia
- ☐ E. Tibial tubercle

Submit



A 13-year-old boy is brought to the office due to right knee pain. Several weeks ago, he developed mild anterior knee pain that has gradually worsened and now causes him to limp. The pain has significantly limited his participation in basketball practice. It is relieved by rest and can be reproduced when the patient straightens out his right knee while seated in a chair. Further evaluation reveals an avulsion fracture affecting a developing secondary ossification center due to muscle overuse. Which of the following structures is most likely involved in this patient's disease process?

- ☐ A. Anterior intercondylar area (10%)
- ☐ B. Anteromedial tibia shaft (11%)
- ☐ C. Fibular head (8%)
- ☐ D. Medial condyle of tibia (11%)
- ☒ E. Tibial tubercle (57%)

Correct



57%

Answered correctly



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02/05/2021

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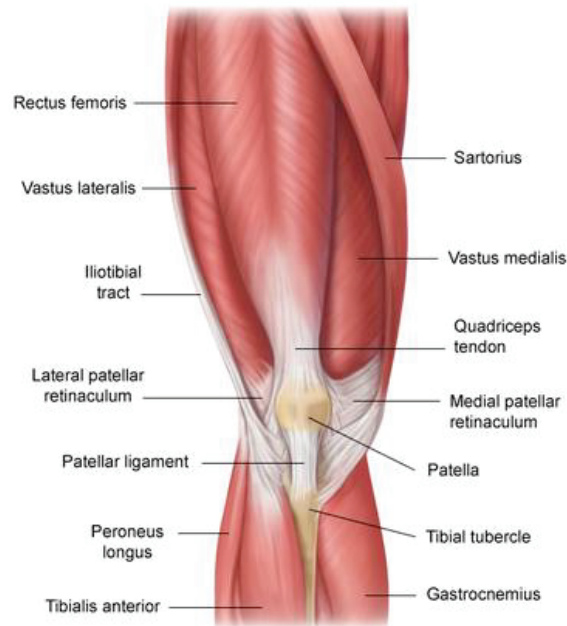
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Anterior knee anatomy



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This patient likely has **Osgood-Schlatter disease** (OSD), a common cause of knee pain in **adolescent athletes** due to overuse of the quadriceps muscle group (ie, rectus femoris, vastus intermedius, vastus medialis, vastus lateralis). The quadriceps is responsible for leg extension at the knee and inserts into the **tibial tubercle** via the patellar ligament. The tubercle forms as a **secondary ossification center** (apophysis) of the tibia, and the cartilaginous nature of the developing tibial tuberosity in childhood makes it more prone to injury compared to the fully ossified bone in adults.

OSD most commonly occurs after a **growth spurt** due to increased tension in tendons and ligaments caused by the rapidly elongating bone. Repetitive quadriceps contraction (eg, sports activity) then results in chronic avulsion of the tibial tubercle. Clinical findings include tenderness and swelling at the tibial tubercle and pain that **worsens with knee extension** (eg, jumping). Imaging frequently shows an elevated and fragmented **tibial tubercle**.

(Choice A) The anterior intercondylar area (ie, fossa) is the space between the medial and lateral condyles of the tibia. The anterior cruciate ligament (ACL) attaches at this specific location and is crucial for knee stabilization. **ACL injury** typically results from sudden deceleration with direction change and presents as acute knee pain, swelling, and instability that prevents weight-bearing.



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Osgood-Schlatter disease



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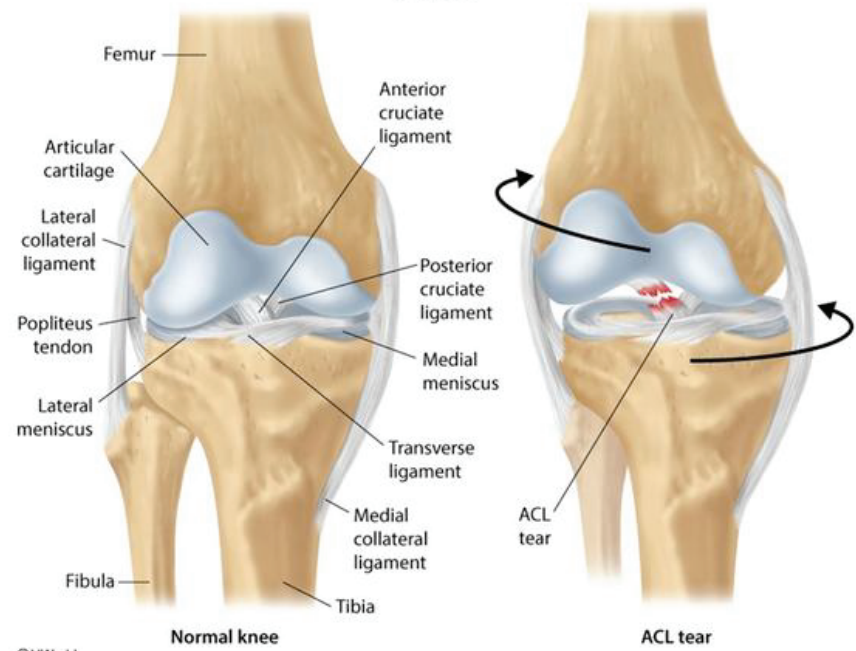
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ACL tear



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presents as acute knee pain, swelling, and instability that prevents weight-bearing.

(Choice B) The sartorius muscle is the longest muscle in the body. It originates from the anterior superior iliac spine and inserts with the [pes anserinus](#) onto the anteromedial tibia shaft near the tibial tuberosity. Pes anserinus bursitis commonly occurs in runners and causes anteromedial knee pain.

(Choices C and D) The tendon of the biceps femoris (part of the hamstrings) inserts at the styloid process of the head of the fibula. The medial condyle of the tibia is the insertion site for the semimembranous muscle, the most medial of the hamstring muscles. The hamstring muscles are involved in knee flexion and hip extension.

Educational objective:

The quadriceps muscle group is connected to the patella, which is attached to the tibial tubercle by the patellar ligament. Repetitive quadriceps contraction (eg, jumping) in adolescents can result in Osgood-Schlatter disease, which is characterized by focal anterior knee pain and swelling due to chronic avulsion of the tibial tubercle.

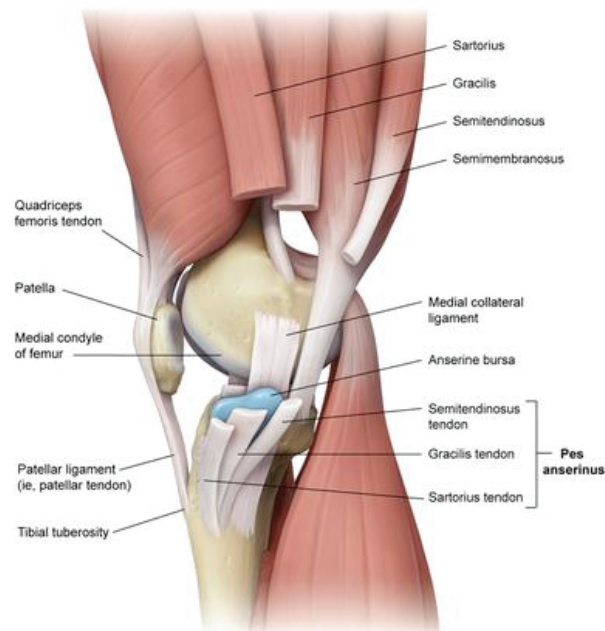
References

- [Precise risk factors for Osgood-Schlatter disease.](#)
- [Osgood Schlatter syndrome.](#)

presents as acute knee pain, swelling, and instability that prevents weight-bearing

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Medial knee & pes anserinus



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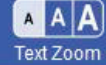
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Researchers are studying treatment of osteoporotic fractures. Subjects with pelvic fractures due to osteoporosis are divided into 2 groups. The control group receives physical therapy along with calcium and vitamin D supplementation. The experimental group receives a parathyroid hormone analogue in addition to the standard therapy. It is found that the subjects who receive hormonal treatment have a shorter time to fracture healing and improved functional outcome. The benefits of the investigational medication are attributed to increased osteoblastic activity. An elevated level of which of the following markers is most likely to reflect the medication effect in these subjects?

- ☐ A. Serum alkaline phosphatase
- ☐ B. Serum aspartate aminotransferase
- ☐ C. Serum calcitonin
- ☐ D. Serum tartrate-resistant acid phosphatase
- ☐ E. Urinary hydroxyproline
- ☐ F. Urinary type I collagen telopeptide



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Feedback



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osteoporosis are divided into 2 groups. The control group receives physical therapy along with calcium and vitamin D supplementation. The experimental group receives a parathyroid hormone analogue in addition to the standard therapy. It is found that the subjects who receive hormonal treatment have a shorter time to fracture healing and improved functional outcome. The benefits of the investigational medication are attributed to increased osteoblastic activity. An elevated level of which of the following markers is most likely to reflect the medication effect in these subjects?

- ✓ ☒ A. Serum alkaline phosphatase (72%)
- ☐ B. Serum aspartate aminotransferase (0%)
- ☐ C. Serum calcitonin (14%)
- ☐ D. Serum tartrate-resistant acid phosphatase (4%)
- ☐ E. Urinary hydroxyproline (3%)
- ☐ F. Urinary type I collagen telopeptide (4%)

Correct

72%



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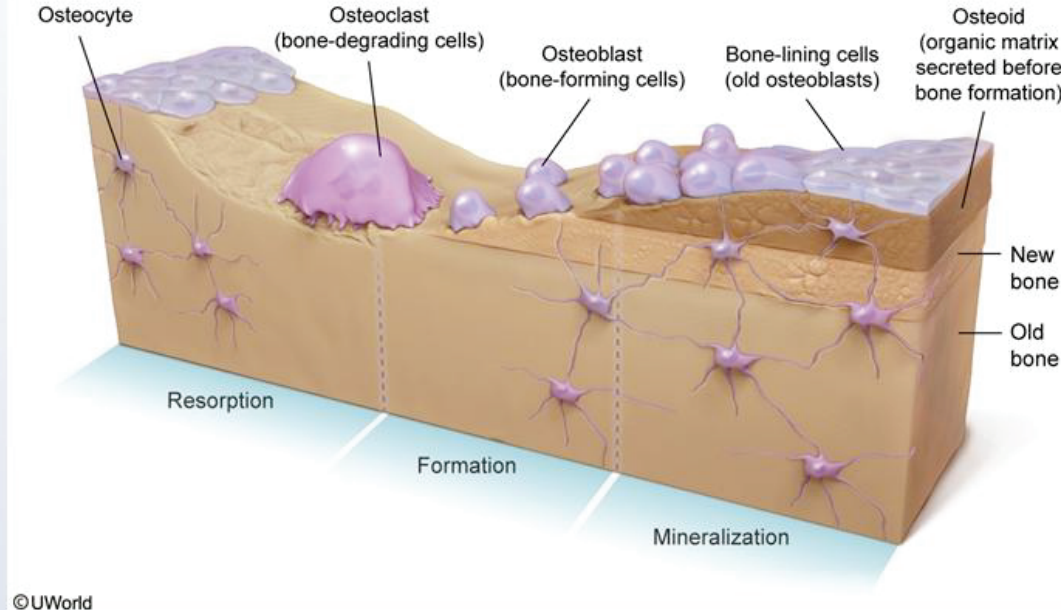
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Bone remodeling



Bone is continually broken down and reformed by the process known as bone remodeling, which consists of the coordinated activity of osteoblasts (responsible for bone formation) and osteoclasts (responsible for



Bone is continually broken down and reformed by the process known as bone remodeling, which consists of the coordinated activity of osteoblasts (responsible for bone formation) and osteoclasts (responsible for bone resorption). The subjects in this study are receiving a **recombinant parathyroid hormone** analog (eg, teriparatide), which promotes **bone formation** by stimulating maturation of pre-osteoblasts into osteoblasts.

Osteoblasts synthesize bone matrix and express **alkaline phosphatase** (AlkP), which promotes normal bone mineralization by increasing local concentrations of inorganic phosphorus. Serum AlkP levels correlate with **osteoblastic activity**. However, total serum levels are nonspecific, as AlkP is also produced by the hepatobiliary tree, intestine, and placenta and may be elevated due to other causes (eg, pregnancy, biliary obstruction). If the source of AlkP is uncertain, AlkP isoenzymes (ie, liver, placental, intestinal, bone) can be differentiated with additional laboratory techniques (eg, electrophoresis, immunoassay). Other markers of osteoblast activity include **N-terminal propeptide of type 1 procollagen** (PINP), which is released during post-translation cleavage of type 1 procollagen before its assembly into mature type 1 collagen fibrils.

(Choice B) Aspartate aminotransferase (AST) is predominantly found in liver, muscle, and kidneys. AST is commonly used as a marker for hepatic injury and is also elevated in rhabdomyolysis and myocardial





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Previous



Next



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Lab Values



Notes



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Settings

collagen fibrils.

(Choice B) Aspartate aminotransferase (AST) is predominantly found in liver, muscle, and kidneys. AST is commonly used as a marker for hepatic injury and is also elevated in rhabdomyolysis and myocardial infarction.

(Choice C) Calcitonin is secreted by the parafollicular C cells of the thyroid and inhibits bone resorption by osteoclasts. As a laboratory marker, calcitonin is primarily used in the diagnosis of medullary thyroid cancer; it does not mark osteoblastic activity.

(Choice D) Acid phosphatase is a family of lysosomal enzymes present in a wide variety of cells, including osteoclasts (the acid phosphatase in osteoclasts is resistant to degradation by tartrate). However, osteoblasts do not express acid phosphatase.

(Choices E and F) Osteoclastic activity (ie, bone resorption) leads to breakdown of fibrillar collagen with release of biomarkers such as hydroxyproline and collagen telopeptides. Increased urine levels are associated with states of increased bone resorption (rather than formation).

Educational objective:

Bone-specific alkaline phosphatase levels correlate with osteoblast activity. Other markers of osteoblast activity include N-terminal propeptide of type 1 procollagen, which is released during post-translation



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Previous



Next



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(Choice C) Calcitonin is secreted by the parafollicular C cells of the thyroid and inhibits bone resorption by osteoclasts. As a laboratory marker, calcitonin is primarily used in the diagnosis of medullary thyroid cancer; it does not mark osteoblastic activity.

(Choice D) Acid phosphatase is a family of lysosomal enzymes present in a wide variety of cells, including osteoclasts (the acid phosphatase in osteoclasts is resistant to degradation by tartrate). However, osteoblasts do not express acid phosphatase.

(Choices E and F) Osteoclastic activity (ie, bone resorption) leads to breakdown of fibrillar collagen with release of biomarkers such as hydroxyproline and collagen telopeptides. Increased urine levels are associated with states of increased bone resorption (rather than formation).

Educational objective:

Bone-specific alkaline phosphatase levels correlate with osteoblast activity. Other markers of osteoblast activity include N-terminal propeptide of type 1 procollagen, which is released during post-translation cleavage of type 1 procollagen.

References

- [International Osteoporosis Foundation and International Federation of Clinical Chemistry and Laboratory Medicine position on bone marker standards in osteoporosis.](https://t.me/USMLEWorldStep1)



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Previous



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Settings

A 34-year-old man comes to the office due to progressive low back pain for several years. The patient reports that the stiffness and pain are worst in the morning but gradually improve during the day. Lately, he has been taking over-the-counter ibuprofen, which provides some relief. Laboratory evaluation shows a positive HLA-B27 antigen. X-ray imaging reveals fusion of the sacroiliac joints. Which of the following is most helpful to monitor disease progression in this patient?

- ☐ A. Degree of chest expansion
- ☐ B. Hand joint mobility
- ☐ C. Peak expiratory flow rate
- ☐ D. Rheumatoid factor level
- ☐ E. Urine protein level

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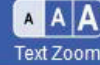
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Settings

A 34-year-old man comes to the office due to progressive low back pain for several years. The patient reports that the stiffness and pain are worst in the morning but gradually improve during the day. Lately, he has been taking over-the-counter ibuprofen, which provides some relief. Laboratory evaluation shows a positive HLA-B27 antigen. X-ray imaging reveals fusion of the sacroiliac joints. Which of the following is most helpful to monitor disease progression in this patient?

- ✓ ☒ A. Degree of chest expansion (40%)
- ☐ B. Hand joint mobility (16%)
- ☐ C. Peak expiratory flow rate (11%)
- ☐ D. Rheumatoid factor level (20%)
- ☐ E. Urine protein level (10%)

Correct



40%

Answered correctly



40 secs

Time Spent



01/15/2021

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End Block

Symptoms/signs of ankylosing spondylitis

- Low back pain (onset age <40, insidious onset, improves with exercise but not with rest, pain at night)
- Hip & buttock pain
- Limited chest expansion & spinal mobility
- Enthesitis (inflammation at the site of insertion of a tendon to the bone)
- Systemic symptoms (eg, fever, chills, fatigue, weight loss)
- Acute anterior uveitis (unilateral pain, photophobia, blurry vision)

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The symptoms of low back pain and morning stiffness in a young man suggest **ankylosing spondylitis** (AS), a chronic inflammatory condition associated with the HLA-B27 serotype. AS is characterized by stiffness and fusion (**ankylosis**) of the axial joints. The **sacroiliac** and apophyseal joints of the spine are the most commonly affected, leading to restricted spinal mobility. Many patients also develop peripheral arthritis and **enthesitis**, which is defined as pain, tenderness, and swelling at the sites of tendon insertion into bone (eg, Achilles tendon insertion).

In addition, AS can cause complications in extraskeletal systems:



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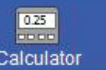
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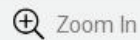
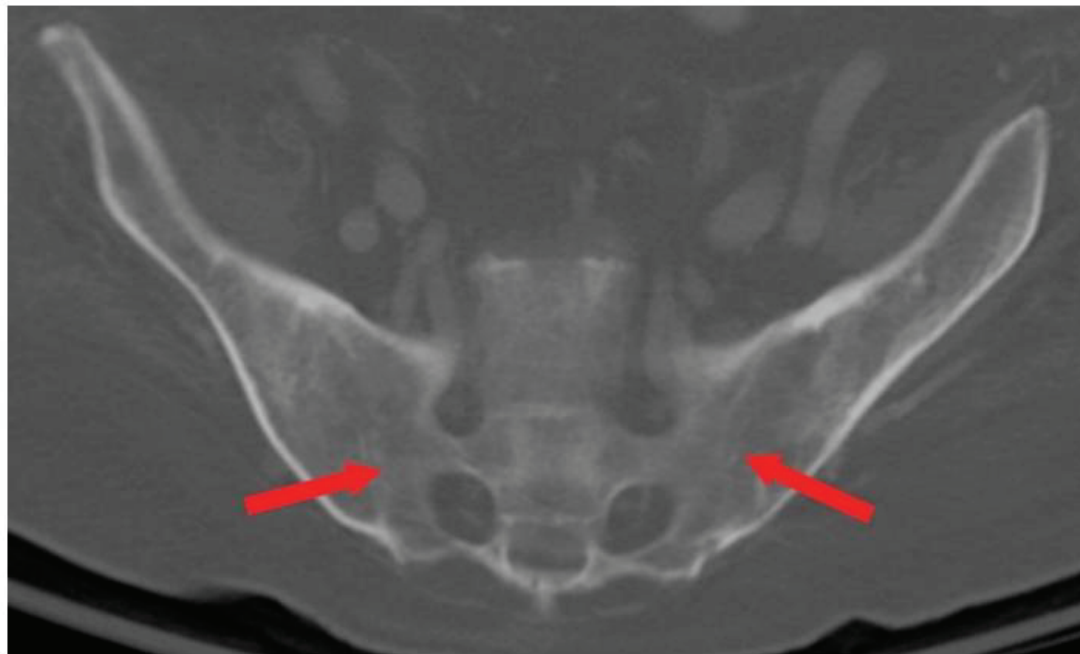


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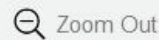


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In addition, AS can cause complications in extraskeletal systems.

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In addition, AS can cause complications in extraskeletal systems:

1. **Respiratory:** Involvement of the thoracic spine and enthesopathies of the costovertebral and costosternal junctions can limit chest wall expansion, leading to hypoventilation. Chest expansion should be monitored regularly in patients with AS.
2. **Cardiovascular:** The most common cardiovascular complication of AS is ascending aortitis, which can lead to dilation of the aortic ring and aortic insufficiency.
3. **Eye:** Anterior uveitis develops in some patients with AS and presents with pain, blurred vision, photophobia, and conjunctival erythema.

(Choice B) Hand joint mobility testing is part of the assessment of rheumatoid arthritis severity. However, the small joints of the hands are not prominently affected by AS.

(Choice C) Peak expiratory flow is determined by airway resistance (obstruction) and chest and abdominal wall muscular function. These variables are not affected by chest wall restriction and are normal in AS. Regular measurement of expiratory flow rates is important in patients with asthma.

(Choice D) Rheumatoid factor can be found in a variety of rheumatic (eg, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus [SLE]) and nonrheumatic disorders (eg, hepatitis C) and in up to 4% of young and healthy individuals. However, it is not associated with AS.



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Next

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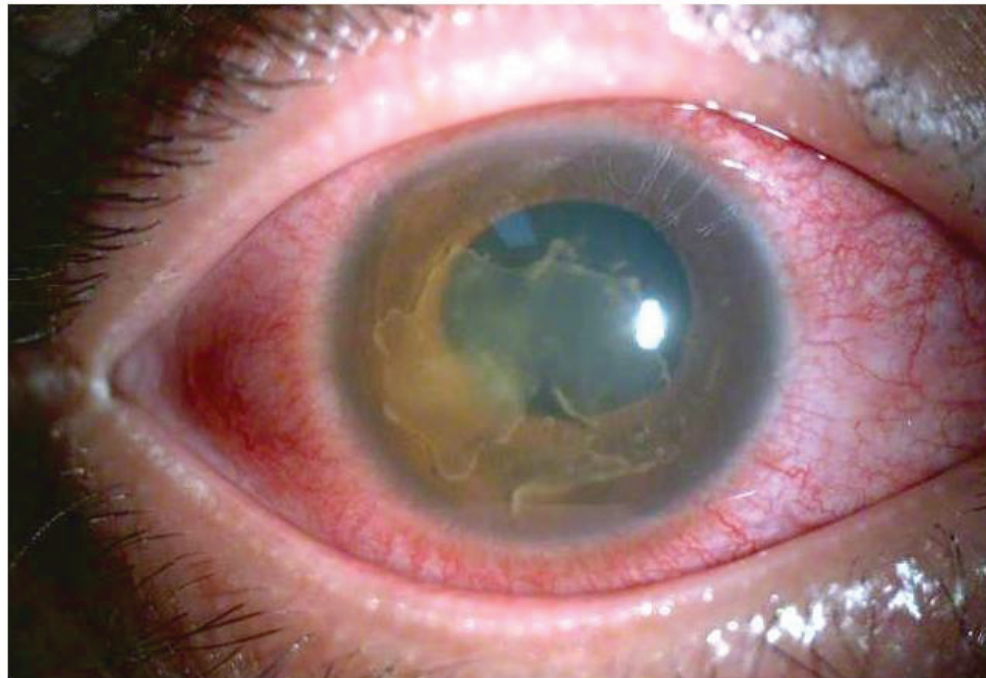
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In addition, AS can cause complications in extraocular muscles.

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Previous

Next

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wall muscular function. These variables are not affected by chest wall restriction and are normal in AS.

Regular measurement of expiratory flow rates is important in patients with asthma.

(Choice D) Rheumatoid factor can be found in a variety of rheumatic (eg, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus [SLE]) and nonrheumatic disorders (eg, hepatitis C) and in up to 4% of young and healthy individuals. However, it is not associated with AS.

(Choice E) Urine protein excretion should be monitored in SLE and diabetes mellitus. Renal involvement is rare in AS.

Educational objective:

Ankylosing spondylitis is characterized by stiffness and fusion of axial joints (ankylosis) and inflammation at the site of insertion of tendons into bone (enthesitis). Involvement of the thoracic spine and costovertebral and costosternal junctions can limit chest wall expansion, leading to hypoventilation.

References

- Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study.

Pathophysiology

Rheumatology/Orthopedics & Sports

Ankylosing spondylitis

Subject

System

Topic

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Feedback



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A 33-year-old woman comes to the office due to swelling affecting her extremities. Over the last 12 months her fingers, arms, and legs have become progressively swollen and somewhat itchy. Physical examination shows diffuse skin thickening extending proximally to the arms, thighs, and trunk. A skin biopsy is performed. Histologic sections show expansion of the dermal layer with atrophy of the intradermal adipose tissue and dermal appendages. High-power images of the dermis demonstrate extensive deposition of dense, eosinophilic connective tissue. This patient is most at risk for which of the following conditions?

- ☐ A. Atlantoaxial subluxation
- ☐ B. Glomerulonephritis
- ☐ C. Interstitial lung disease
- ☐ D. Non-Hodgkin lymphoma
- ☐ E. Ulcerative colitis

Submit



A 33-year-old woman comes to the office due to swelling affecting her extremities. Over the last 12 months her fingers, arms, and legs have become progressively swollen and somewhat itchy. Physical examination shows diffuse skin thickening extending proximally to the arms, thighs, and trunk. A skin biopsy is performed. Histologic sections show expansion of the dermal layer with atrophy of the intradermal adipose tissue and dermal appendages. High-power images of the dermis demonstrate extensive deposition of dense, eosinophilic connective tissue. This patient is most at risk for which of the following conditions?

- ☐ A. Atlantoaxial subluxation (6%)
- ☐ B. Glomerulonephritis (19%)
- ☒ C. Interstitial lung disease (56%)
- ☐ D. Non-Hodgkin lymphoma (6%)
- ☐ E. Ulcerative colitis (10%)

Correct



56%

Answered correctly



01 min, 42 secs

Time Spent



12/21/2020

Last Updated

Block Time Remaining: 00:14:26

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Feedback



Suspend



End Block

Systemic sclerosis

| | Limited cutaneous | Diffuse cutaneous |
|----------------|---|--|
| Manifestations | <ul style="list-style-type: none">• Distal sclerosis (most prominent in the fingers)• CREST syndrome | <ul style="list-style-type: none">• Proximal sclerosis (involves the trunk & proximal extremities) |
| Serology | <ul style="list-style-type: none">• Anticentromere | <ul style="list-style-type: none">• Anti-SCL-70 |
| Complications | <ul style="list-style-type: none">• Pulmonary hypertension | <ul style="list-style-type: none">• Interstitial lung disease• Scleroderma renal crisis |

Anti-SCL-70 = anti-topoisomerase I; **CREST** = **C**alcinosis cutis, **R**aynaud phenomenon, **E**sophageal dysmotility, **S**clerodactyly, **T**elangiectasia.

This patient has diffuse skin thickening consistent with **systemic sclerosis** (SS), an autoimmune disease characterized by widespread **fibrosis** of multiple organ systems. Early symptoms often include swelling of the fingers and mild pruritus. A characteristic skin biopsy finding is **dermal layer expansion** due to diffuse deposition of collagen (eosinophilic connective tissue), resulting in **atrophy** of the **intradermal adipose tissue and dermal appendages** (i.e. hair follicles, glands).



the fingers and mild pruritus. A characteristic skin biopsy finding is **dermal layer expansion** due to diffuse deposition of collagen (eosinophilic connective tissue), resulting in **atrophy** of the **intradermal adipose** tissue and **dermal appendages** (ie, hair follicles, glands).

Up to 80% of patients with SS develop pulmonary complications, with the incidence depending on the SS subtype:

- **Interstitial lung disease** is the most common pulmonary complication of **diffuse cutaneous SS** (ie, skin involvement extends proximal to the wrist and may include the trunk).
- **Pulmonary hypertension** is the most common pulmonary complication of limited cutaneous SS (ie, skin involvement is mainly in the hands and/or face), which is often associated with **CREST syndrome**.

(Choice A) Atlantoaxial subluxation is a feared complication of rheumatoid arthritis, as significant neck extension (eg, during intubation) can result in dislocation and spinal cord injury. Rheumatoid arthritis typically presents with pain and swelling of the small joints of the hands and wrists; histology reveals synovial hyperplasia.

(Choice B) SS is associated with scleroderma renal crisis; however, this occurs due to renal vascular injury, not glomerulonephritis. Scleroderma renal crisis often presents as hypertensive emergency with



Exhibit Display

CREST syndrome characteristics

Calcinosis
Raynaud phenomenon
Esophageal dysmotility
Sclerodactyly
Telangiectasias

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(Choice B) SS is associated with scleroderma renal crisis; however, this occurs due to renal vascular injury, not glomerulonephritis. Scleroderma renal crisis often presents as hypertensive emergency with signs of end-organ dysfunction; casts (which are typical in glomerulonephritis) are characteristically absent.

(Choice D) Non-Hodgkin lymphoma is a potential complication of Sjögren syndrome, which typically presents with dry mouth and eyes. Labial salivary gland biopsy demonstrates **extensive lymphoid infiltrate** with atrophy of the acinar gland.

(Choice E) Ulcerative colitis is often associated with ankylosing spondylitis. Although dactylitis (ie, sausage fingers) can occur with this condition, skin thickening and collagen deposition would be unexpected.

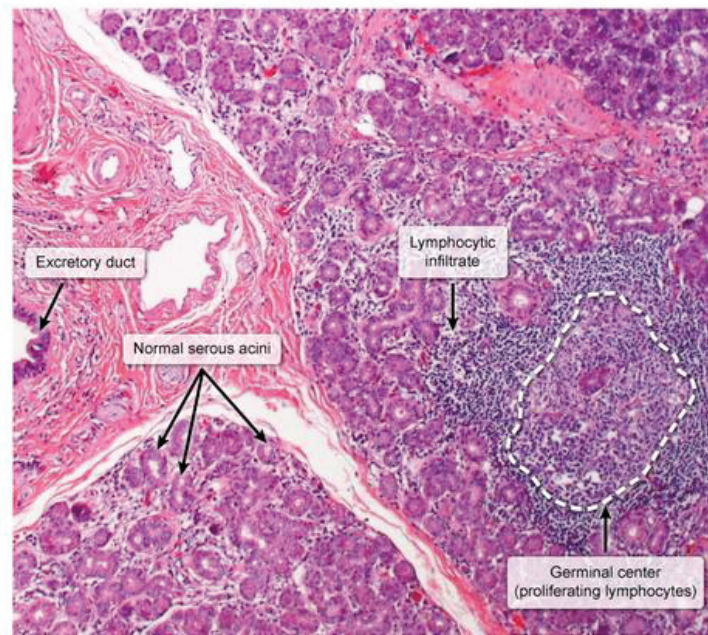
Educational objective:

Systemic sclerosis (SS) is an autoimmune disease characterized by the widespread fibrosis of multiple organ systems. Histology demonstrates expansion of the dermal layer with diffuse collagen deposition and atrophy of the intradermal adipose tissue and dermal appendages. Pulmonary complications are common (eg, interstitial lung disease, pulmonary hypertension).



Exhibit Display

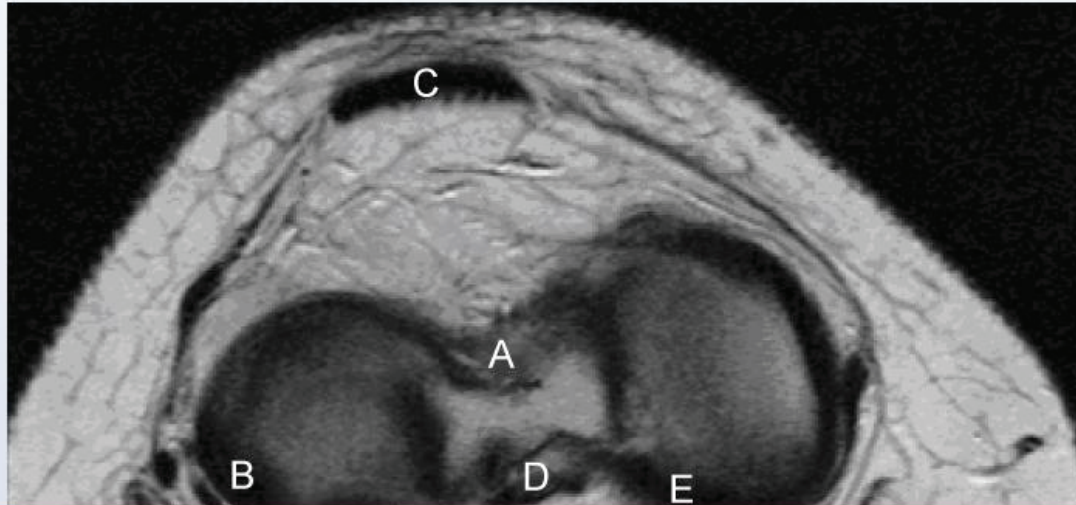
Sjogren syndrome



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A 20-year-old man comes to the hospital with knee pain after he tripped and landed on his right knee during a soccer game. The anterior portion of his tibia impacted directly against the ground, and he has been unable to bear weight since the injury. On physical examination, the patient's knee appears swollen, and there is excessive posterior displacement of the tibia when pressure is applied to his anterior tibia with the knee in the flexed position. An axial MRI cross section of the right knee at the level of the tibial plateau is shown below. Which of the following structures is most likely injured in this patient?





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Previous



Next



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Tutorial



Lab Values



Notes



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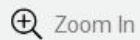
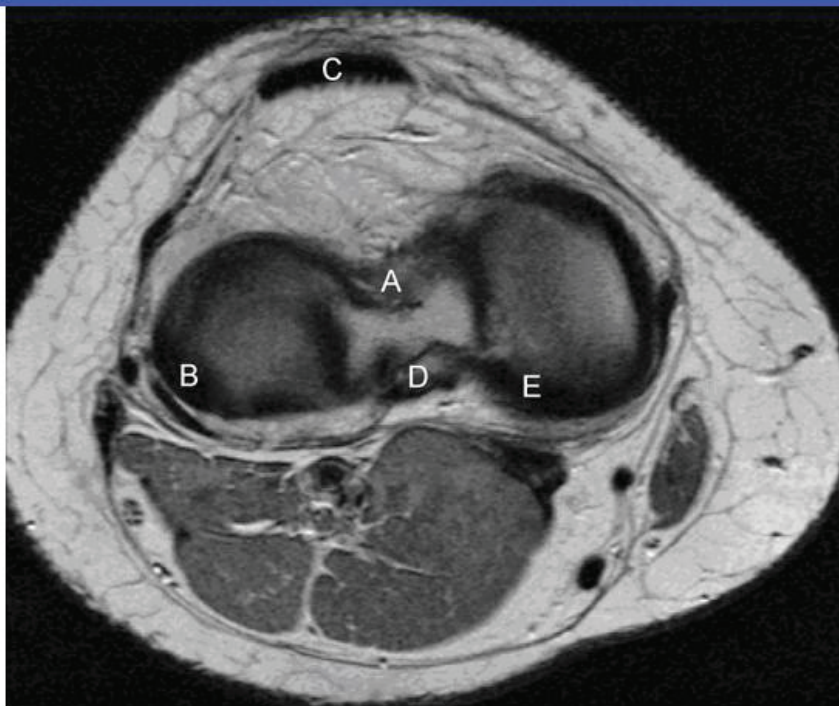


Text Zoom

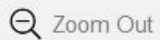


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Suspend



End Block



Mark



Previous



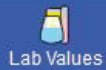
Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



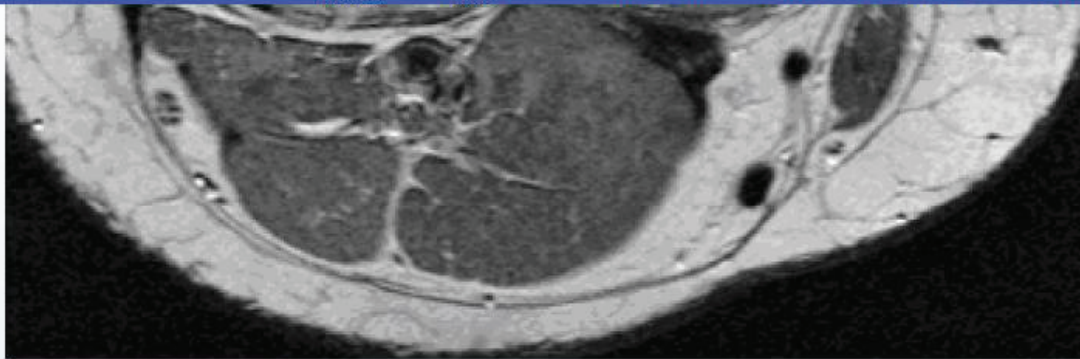
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Settings

☐ A.A☒ B.B☐ C.C☐ D.D☐ E.E**Submit**

1



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

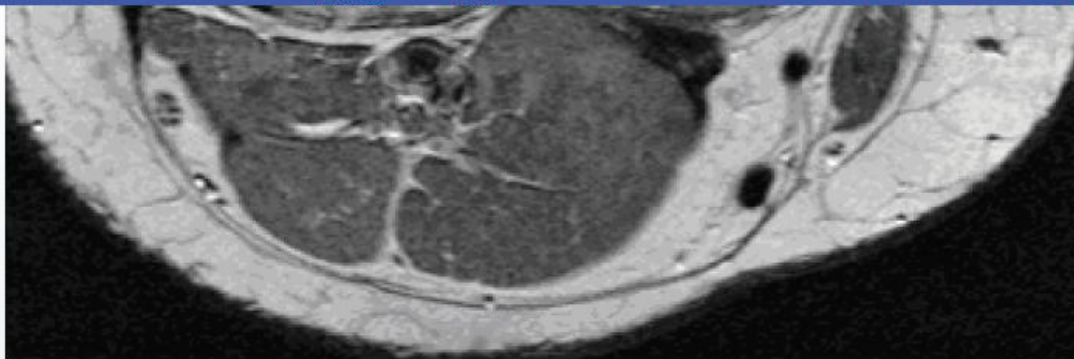
Notes

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- ☐ A.A (16%)
- ☐ B.B (1%)
- ☐ C.C (1%)
- ☒ D.D (77%)
- ☐ E.E (2%)

Correct

77%



01 min, 28 secs



02/02/2021

Block Time Remaining: 00:15:54

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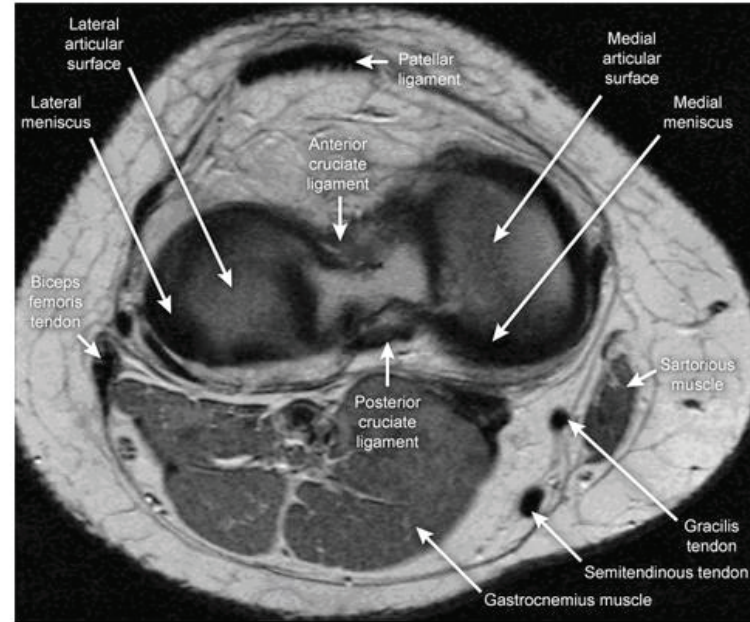
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Exhibit Display

Knee MRI



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The **anterior cruciate ligament** (ACL) and the **posterior cruciate ligament** (PCL) are found within the articular capsule of the knee joint and **cross one another** as they span from the femur to the tibia. The PCL originates from the anterolateral surface of the medial femoral condyle and inserts into the posterior intercondylar area of the tibia. At the level of the tibial plateau (as seen on the **axial MRI** above), the ACL is anterior, and the **PCL is posterior**. The ACL functions to resist anterior displacement of the tibia relative to the femur (**Choice A**).

The PCL prevents **posterior displacement** of the tibia relative to the femur, and its integrity can be tested by using the **posterior drawer test** (posterior force applied to the tibia while the knee is flexed). **PCL tears** most commonly occur following a direct blow to the anterior proximal tibia during sporting activities or motor vehicle collisions.

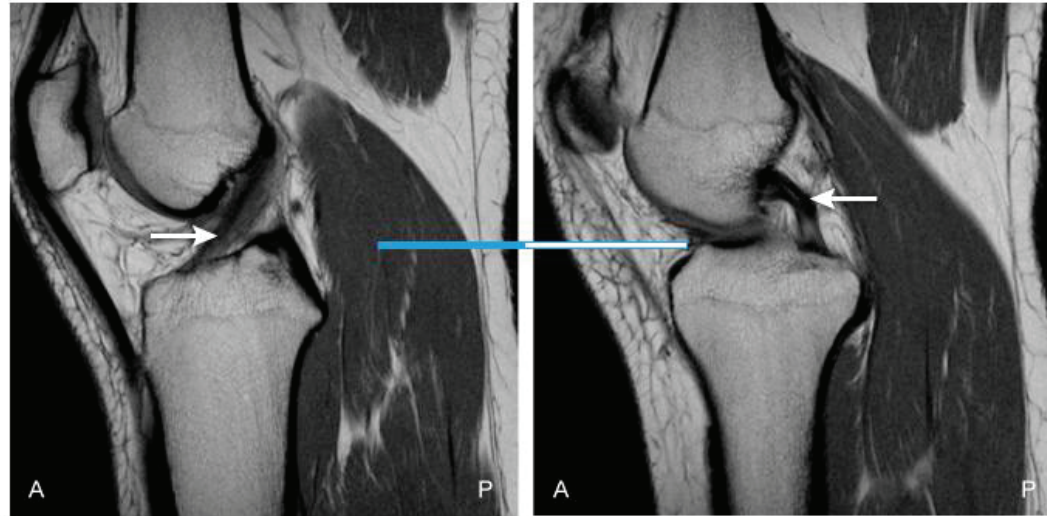
(Choices B and E) The medial and lateral menisci are crescent-shaped bands of cartilaginous tissue that line the periphery of the knee joint. Meniscal tears are associated with twisting of a flexed knee while the corresponding foot is planted. Meniscal damage can be detected on physical examination by joint-line tenderness during provocative maneuvers (eg, **McMurray test**).

(Choice C) The patellar ligament (ie, patellar tendon) connects the inferior portion of the patella to the tibial tuberosity. Patellar ligament rupture is associated with underlying ligamentous damage (eg,

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Anterior cruciate ligament

Posterior cruciate ligament



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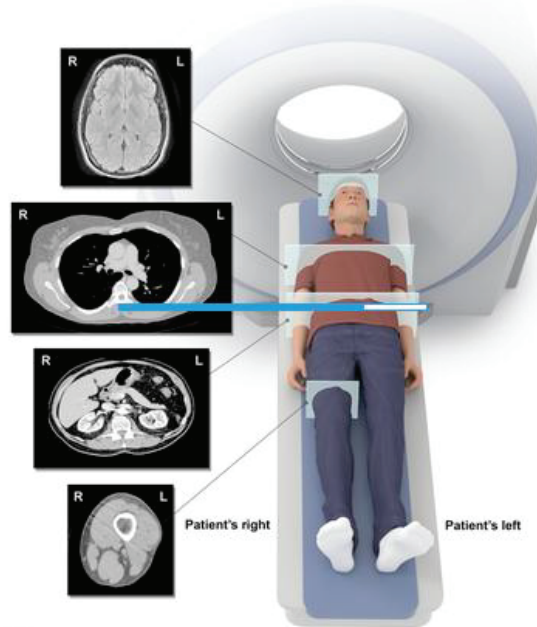
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Exhibit Display

Axial CT/MRI orientation



Zoom In

Zoom Out

Reset

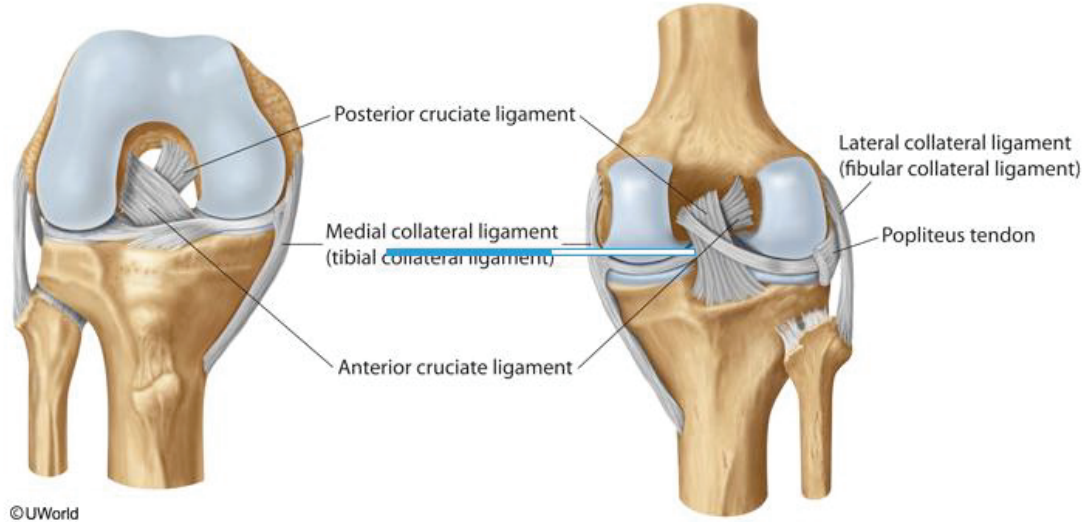
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Anterior view

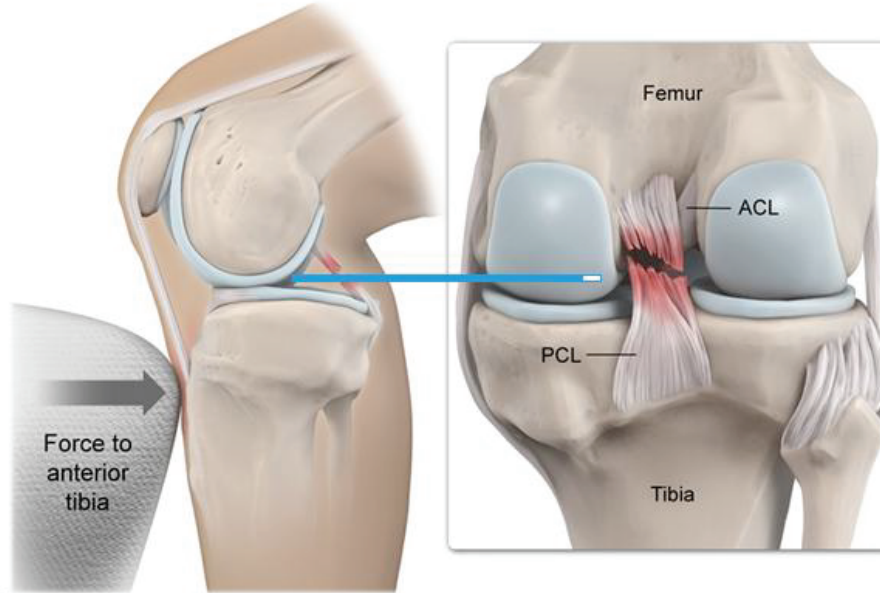
Posterior view



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Exhibit Display

Posterior cruciate ligament tear



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Zoom In

Zoom Out

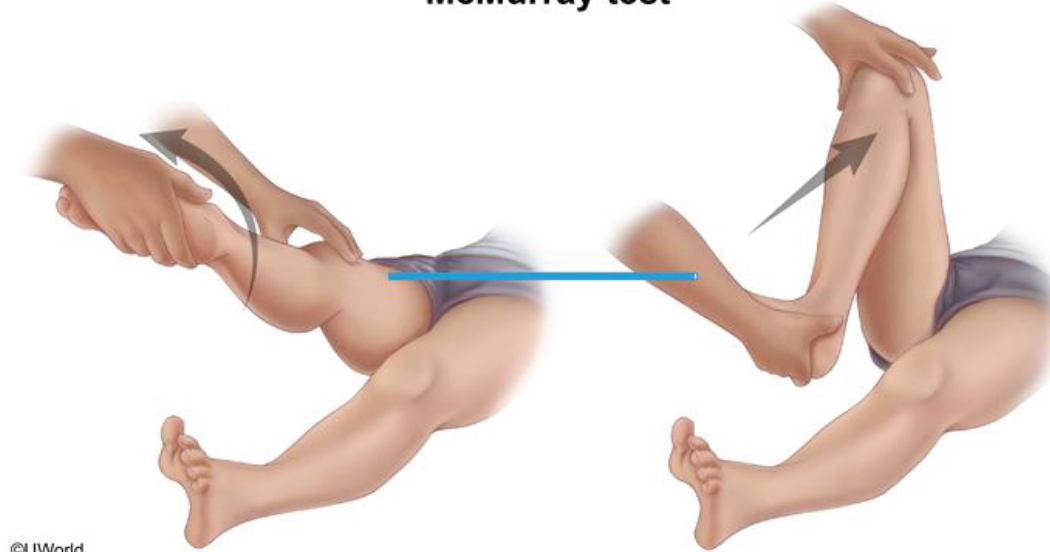
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New | Existing

My Notebook

Exhibit Display

McMurray test



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Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

corresponding foot is planted. Meniscal damage can be detected on physical examination by joint-line tenderness during provocative maneuvers (eg, [McMurray test](#)).

(Choice C) The patellar ligament (ie, patellar tendon) connects the inferior portion of the patella to the tibial tuberosity. Patellar ligament rupture is associated with underlying ligamentous damage (eg, autoimmune disease, overuse injury) and usually occurs following forceful contraction of the quadriceps muscles while the knee is flexed (eg, landing after a jump). A complete patellar ligament tear would result in swelling and a high-riding patella on physical examination.

Educational objective:

The posterior cruciate ligament prevents posterior displacement of the tibia relative to the femur. It originates from the anterolateral surface of the medial femoral condyle and inserts into the posterior intercondylar area of the tibia. Its integrity can be tested in the clinical setting by using the posterior drawer test.

Anatomy

Rheumatology/Orthopedics & Sports

Knee trauma

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 34-year-old man comes to the physician due to painful urination. Physical examination shows a watery penile discharge. Urethral swabs obtained from the patient are negative for gonococcal infection. He is treated appropriately and his symptoms resolve. Two weeks later, he develops acute conjunctivitis, right knee pain, and vesicular rash on his palms and soles. This patient's condition is most likely associated with which of the following?

- ☐ A. Esophageal dysmotility
- ☐ B. Hyperparathyroidism
- ☐ C. Polymyositis
- ☐ D. Sacroiliitis
- ☐ E. Tabes dorsalis

Submit

1



Feedback



Suspend



End Block



A 34-year-old man comes to the physician due to **painful urination**. Physical examination shows a **watery penile discharge**. Urethral swabs obtained from the patient are negative for gonococcal infection. He is treated appropriately and his symptoms resolve. Two weeks later, he develops **acute conjunctivitis**, right **knee pain**, and vesicular rash on his palms and soles. This patient's condition is most likely associated with which of the following?

- ☐ A. Esophageal dysmotility (3%)
- ☐ B. Hyperparathyroidism (0%)
- ☐ C. Polymyositis (11%)
- ☒ D. Sacroiliitis (48%)
- ☐ E. Tabes dorsalis (35%)

Correct



48%
Answered correctly



01 min, 19 secs
Time Spent



12/25/2020
Last Updated



Reactive arthritis

| | |
|--------------------------------|--|
| Preceding infection | <ul style="list-style-type: none">• Genitourinary infection: <i>Chlamydia trachomatis</i>• Enteritis: <i>Salmonella, Shigella, Yersinia, Campylobacter, Clostridioides</i> (formerly <i>Clostridium</i>) <i>difficile</i> |
| Musculoskeletal | <ul style="list-style-type: none">• Asymmetric oligoarthritis• Enthesitis• Dactylitis |
| Extraarticular symptoms | <ul style="list-style-type: none">• Ocular: conjunctivitis, anterior uveitis• Genital: urethritis, cervicitis, prostatitis• Dermal: keratoderma blennorrhagicum, circinate balanitis• Oral ulcers |

Urethritis, conjunctivitis, and mono- or oligoarticular arthritis constitute the classic triad of **reactive arthritis (ReA)**. This seronegative (rheumatoid factor-negative) spondyloarthropathy most commonly affects patients age 20-40 and is associated with **HLA-B27**. Symptoms generally manifest 1-4 weeks



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

- Oral ulcers

Urethritis, conjunctivitis, and mono- or oligoarticular arthritis constitute the classic triad of **reactive arthritis (ReA)**. This seronegative (rheumatoid factor-negative) spondyloarthropathy most commonly affects patients age 20-40 and is associated with **HLA-B27**. Symptoms generally manifest 1-4 weeks following a primary infection causing urethritis or enteritis and are caused by an autoimmune reaction initiated by the infecting pathogen. Skin findings include keratoderma blennorrhagicum (hyperkeratotic vesicles on the palms and soles) and circinate balanitis (serpiginous annular dermatitis of the glans penis). Axial involvement, including **sacroiliitis**, may occur in about 20% of cases.

(Choice A) Esophageal dysmotility is a classic finding in scleroderma although it can occur in other conditions.

(Choice B) Hyperparathyroidism may occur in the setting of multiple endocrine neoplasia.

(Choice C) Polymyositis may occur in the setting of dermatomyositis or as a separate entity.

(Choice E) Tabes dorsalis is a manifestation of tertiary syphilis. Secondary syphilis causes maculopapular or pustular (but not vesicular) rash that can involve the palms and soles; it is generally associated with polyarthritis (mono-arthritis is very rare).



1



Feedback



Suspend



End Block

(Choice A) Esophageal dysmotility is a classic finding in scleroderma although it can occur in other conditions.

(Choice B) Hyperparathyroidism may occur in the setting of multiple endocrine neoplasia.

(Choice C) Polymyositis may occur in the setting of dermatomyositis or as a separate entity.

(Choice E) Tabes dorsalis is a manifestation of tertiary syphilis. Secondary syphilis causes maculopapular or pustular (but not vesicular) rash that can involve the palms and soles; it is generally associated with polyarthritis (mono-arthritis is very rare).

Educational objective:

The classic triad of reactive arthritis is nongonococcal urethritis, conjunctivitis, and arthritis. It is an HLA-B27-associated arthropathy that occurs within several weeks following a genitourinary or enteric infection. It belongs to the group of seronegative spondyloarthropathies (including ankylosing spondylitis) and can cause sacroiliitis in about 20% of cases.

Pathophysiology
Subject

Rheumatology/Orthopedics & Sports
System

Reactive arthritis
Topic



An 18-year-old soccer player is evaluated for difficulty ambulating and right thigh pain. He has no other medical conditions and takes no medications. On examination, active and passive hip flexion and knee extension are impaired. Extension, abduction, and adduction at the hip are intact and knee flexion is also intact. Which of the following muscles is most likely injured in this patient?

- ☐ A. Biceps femoris long head
- ☐ B. Psoas muscle
- ☐ C. Rectus femoris
- ☐ D. Sartorius
- ☐ E. Tensor fascia lata

Submit



An 18-year-old soccer player is evaluated for difficulty ambulating and right thigh pain. He has no other medical conditions and takes no medications. On examination, active and passive hip flexion and knee extension are impaired. Extension, abduction, and adduction at the hip are intact and knee flexion is also intact. Which of the following muscles is most likely injured in this patient?

- ☐ A. Biceps femoris long head (14%)
- ☐ B. Psoas muscle (18%)
- ☒ C. Rectus femoris (50%)
- ☐ D. Sartorius (11%)
- ☐ E. Tensor fascia lata (4%)

IncorrectCorrect answer
C50%
Answered correctly01 min, 35 secs
Time Spent02/21/2021
Last Updated

Explanation

Block Time Remaining: 00:18:49

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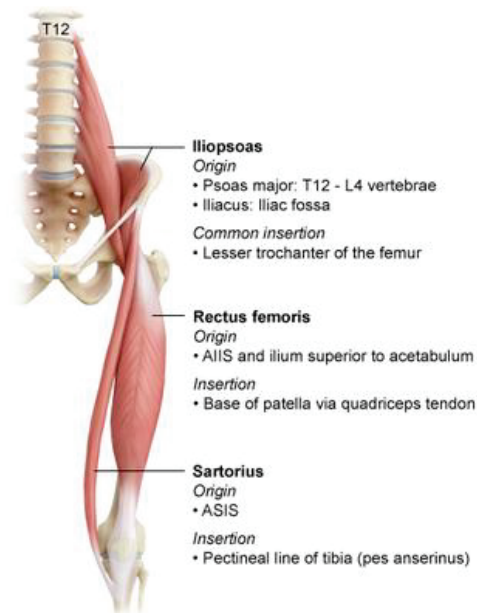
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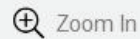
Exhibit Display

Muscular attachments of the major hip flexors

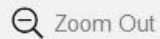


*AIIS = anterior inferior iliac spine; ASIS = anterior superior iliac spine

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The major muscles responsible for **hip flexion** are the **rectus femoris**, **iliopsoas**, and **sartorius**. These muscles originate on the pelvis and spinal column and cross the hip joint anteriorly, giving them the capacity to carry out this motion. This patient has impairment not only with hip flexion but also with knee extension. Of these muscles, only the sartorius and rectus femoris (part of quadriceps femoris) also cross the knee and therefore can influence both hip and knee movements.

The **rectus femoris** originates from the anterior inferior iliac spine and the ilium and inserts at the base of the patella via the quadriceps tendon, allowing it to flex the hip and **also extend the knee** upon contraction. The rectus femoris (and quadriceps as a whole) also provides stability and control during ambulation, deceleration (eg, landing a jump), and rapid changes in movement (eg, cutting in soccer).

In contrast, the sartorius originates from the anterior superior iliac spine and crosses the anterior thigh to insert at the superomedial surface of the tibia. Because of its oblique orientation across the anterior thigh, the **sartorius** is responsible for hip flexion, external rotation, and abduction as well as **knee flexion** (not extension) (**Choice D**). This combination of movements is needed to sit in a cross-legged position.

(**Choice A**) The biceps femoris, along with semitendinosus and semimembranosus, form the **hamstring muscle group** in the posterior thigh that is responsible for *hip extension* and *knee flexion*. These movements are made possible because the long head of biceps femoris originates at the ischial tuberosity.



(Choice A) The biceps femoris, along with semitendinosus and semimembranosus, form the **hamstring muscle group** in the posterior thigh that is responsible for *hip extension* and *knee flexion*. These movements are made possible because the long head of biceps femoris originates at the ischial tuberosity and inserts at the fibular head, crossing both the hip and knee joints.

(Choice B) The psoas muscle originates at T12-L4 vertebrae and inserts at the lesser trochanter of the femur, enabling it to function as a hip flexor. Because it does not cross the knee, it does not contribute to leg movement.

(Choice E) **Tensor fascia lata** is a small muscle along the lateral thigh that originates from the anterior superior iliac spine and inserts in the lateral condyle of the tibia via the iliotibial tract. It works with the **gluteus medius and gluteus minimus** to abduct and medially rotate the hip.

Educational objective:

The rectus femoris, iliopsoas, and sartorius are the major hip flexors. Of these, only the rectus femoris and sartorius also affect knee movement. The sartorius flexes the knee while the rectus femoris extends the knee.

Anatomy

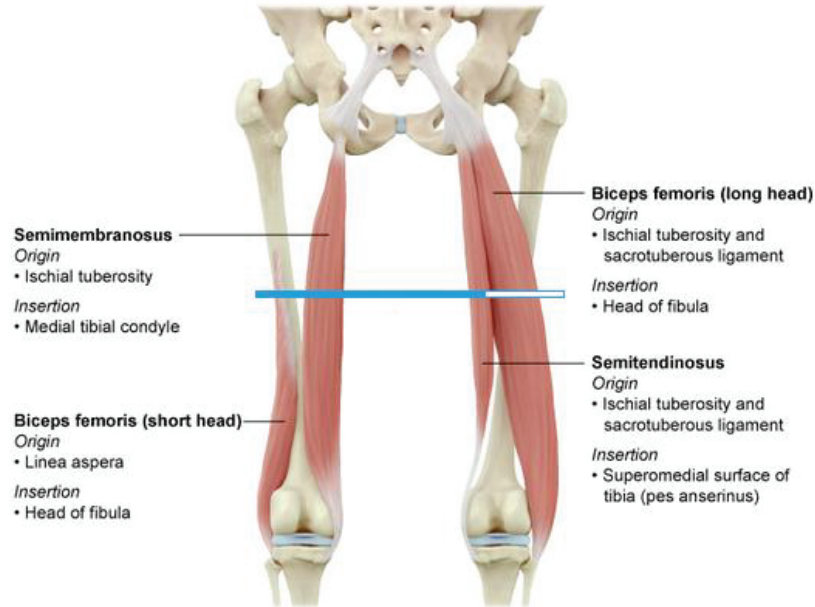
Rheumatology/Orthopedics & Sports

Quadriceps muscle and tendon injuries



Exhibit Display

Major hip extensors and knee flexors

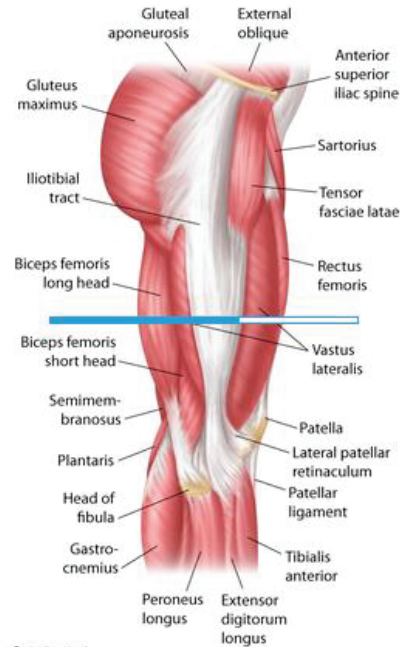


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Exhibit Display

Lateral hip and thigh anatomy



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New | Existing

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Exhibit Display

Gluteal muscle attachments

Gluteus medius

Origin

- Upper gluteal surface of the ilium

Insertion

- Greater trochanter of the femur

Gluteus minimus

Origin

- Lower gluteal surface of the ilium

Insertion

- Greater trochanter of the femur

Gluteus maximus

Origin

- Gluteal surface of the ilium, dorsal sacrum & coccyx, sacrotuberous ligament

Insertion

- Gluteal tuberosity of the femur & the iliotibial tract

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Reset

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A 28-year-old man comes to the office due to a 4-month history of pain and stiffness in the lower back and neck. Symptoms are worse with prolonged rest and in the early morning. The patient also has fatigue and poor sleep. He has no other medical conditions and takes no medications. Vital signs are normal. Examination shows limited forward bending of the trunk. Lower extremity muscle power and reflexes are normal. Which of the following is most likely to confirm the diagnosis?

- ☐ A. Complete blood count
- ☐ B. Erythrocyte sedimentation rate
- ☐ C. Nerve conduction studies
- ☐ D. Rheumatoid factor level
- ☐ E. X-ray of the pelvis

Submit



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

A 28-year-old man comes to the office due to a 4-month history of pain and stiffness in the lower back and neck. Symptoms are worse with prolonged rest and in the early morning. The patient also has fatigue and poor sleep. He has no other medical conditions and takes no medications. Vital signs are normal. Examination shows limited **forward bending** of the **trunk**. Lower extremity muscle power and reflexes are normal. Which of the following is most likely to confirm the diagnosis?

- ☐ A. Complete blood count (1%)
- ☐ B. Erythrocyte sedimentation rate (18%)
- ☐ C. Nerve conduction studies (1%)
- ☐ D. Rheumatoid factor level (11%)
- ☒ E. X-ray of the pelvis (66%)

Correct

 66%
Answered correctly 38 secs
Time Spent 12/16/2020
Last Updated

Block Time Remaining: 00:19:27

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Feedback



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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Ankylosing spondylitis

Pathogenesis

- Altered gut biome/defective mucosal barrier
- Increased production of IL-17, TNF- α & prostaglandins
- Increased risk with HLA-B27

Clinical findings

- Inflammatory back & buttock pain
 - Insidious onset at age <40
 - Relieved with exercise but not rest
 - Nocturnal pain
- Reduced chest expansion & spinal mobility
- Enthesitis (tenderness at tendon insertion sites)
- Dactylitis (swelling of fingers & toes)
- Anterior uveitis

Laboratory/imaging

- Elevated ESR & CRP
- Sacroiliitis: bone erosions, subchondral sclerosis, eventual bony fusion (ankylosis)



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Feedback



Suspend



End Block

Laboratory/imaging

- Elevated ESR & CRP
- Sacroiliitis: bone erosions, subchondral sclerosis, eventual bony fusion (ankylosis)
- Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

HLA-B27 = human leukocyte antigen B27; **TNF- α** = tumor necrosis factor-alpha; **CRP** = C-reactive protein; **ESR** = erythrocyte sedimentation rate.

This patient with **chronic pain and stiffness** in the spine and **reduced spinal mobility** likely has **ankylosing spondylitis (AS)**. The pain in AS is generally better with activity and worse at night and with rest, which can lead to disrupted sleep and daytime fatigue. AS is characterized by bony erosions and excessive formation of new bone in the axial skeleton, primarily around the vertebral margins.

Patients with suspected AS should undergo x-ray of the spine and pelvis, which can assist in the diagnosis:

- **X-ray of the pelvis** shows inflammatory arthritis of the sacroiliac joints (ie, **sacroiliitis**), visible as joint **erosions with subchondral sclerosis**. These findings are **relatively specific** for spondylarthritis (including AS) and, in association with typical symptoms, are often adequate for diagnosis. As the disorder progresses, the joint space is obliterated, leading to bony fusion (**ankylosis**).



Mark



Previous



Next



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Tutorial



Lab Values



Notes



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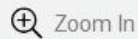
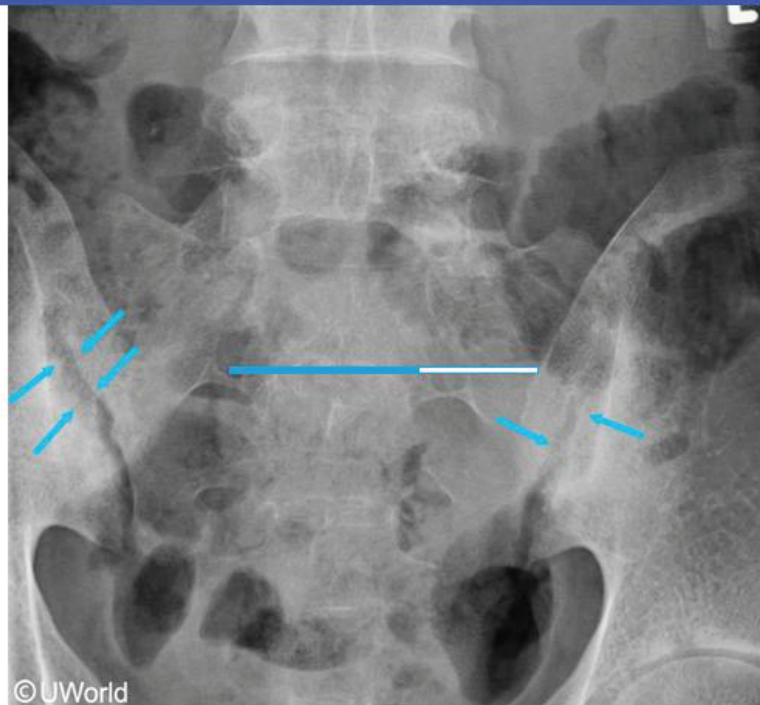


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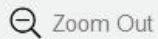


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disorder progresses the joint space is obliterated leading to bony fusion (ankylosis)

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Feedback



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End Block

erosions with subchondral sclerosis. These findings are **relatively specific** for spondylarthritis (including AS) and, in association with typical symptoms, are often adequate for diagnosis. As the disorder progresses, the joint space is obliterated, leading to bony fusion (**ankylosis**).

- **Spinal x-ray** may show heterotopic ossification affecting the margins of the vertebral bodies, which are visible as **bridging syndesmophytes**. Advanced and continuous syndesmophyte formation is termed **bamboo spine**.

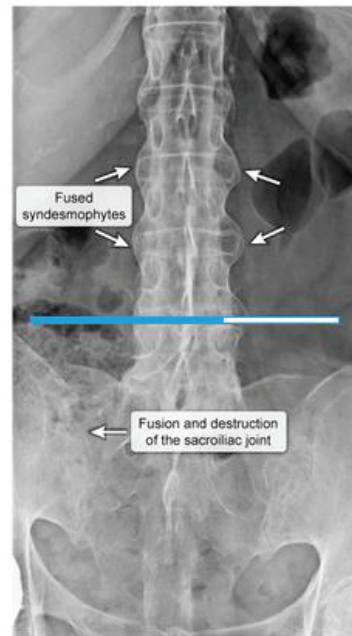
AS is a seronegative spondyloarthropathy, and there are **no serologic tests** to confirm the diagnosis. Although most cases are associated with human leukocyte antigen B27 (HLA-B27), most patients with HLA-B27 never develop AS, so this marker does not confirm the diagnosis. Patients often have elevated inflammatory markers (eg, erythrocyte sedimentation rate, C-reactive protein) and abnormal blood counts (eg, anemia, leukocytosis), but these findings are nonspecific (**Choices A and B**).

(Choice C) Nerve conduction studies are typically used to identify peripheral nerve lesions in patients with deficits on neurologic examination. This patient has normal examination findings, so electrodiagnostics would have little utility.

(Choice D) Rheumatoid factor is used in the diagnosis of rheumatoid arthritis (RA), which typically occurs in patients age >40 and is more common in women (AS is more common in men). RA usually causes a

Exhibit Display

Ankylosing spondylitis (bamboo spine)



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inflammatory markers (eg, erythrocyte sedimentation rate, C-reactive protein) and abnormal blood counts

(eg, anemia, leukocytosis), but these findings are nonspecific (**Choices A and B**).

(Choice C) Nerve conduction studies are typically used to identify peripheral nerve lesions in patients with deficits on neurologic examination. This patient has normal examination findings, so electrodiagnostics would have little utility.

(Choice D) Rheumatoid factor is used in the diagnosis of rheumatoid arthritis (RA), which typically occurs in patients age >40 and is more common in women (AS is more common in men). RA usually causes a symmetric peripheral arthritis; cervical involvement can occur, but the lumbar spine is usually spared.

Educational objective:

Ankylosing spondylitis presents with chronic back pain with reduced spinal mobility. X-rays of the spine and pelvis can aid in diagnosis by identifying specific findings such as sacroiliitis (eg, joint erosions with subchondral sclerosis and eventual ankylosis) and bridging syndesmophytes (heterotopic ossification affecting vertebral body margins).

Pathology
Subject

Rheumatology/Orthopedics & Sports
System

Ankylosing spondylitis
Topic

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A 43-year-old woman comes to the office due to progressive fatigue and intermittent pain in the hands, feet, and knee joints. The pain caused the patient to stop her daily yoga routine 2 months ago, and she has had difficulty performing daily household activities. She has had no fever, rash, or oral ulcers but frequently drinks water or chews gum due to her mouth feeling dry. The patient has no prior medical conditions and takes no medications or herbal supplements. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows no muscle tenderness or joint swelling. The thyroid gland is normal to palpation. There is nontender diffuse swelling of the parotid glands. Laboratory evaluation reveals mild normocytic normochromic anemia and an elevated erythrocyte sedimentation rate. A salivary gland biopsy image representative of this patient's disease process is shown in the [exhibit](#). This patient is at greatest risk for which of the following due to her current condition?

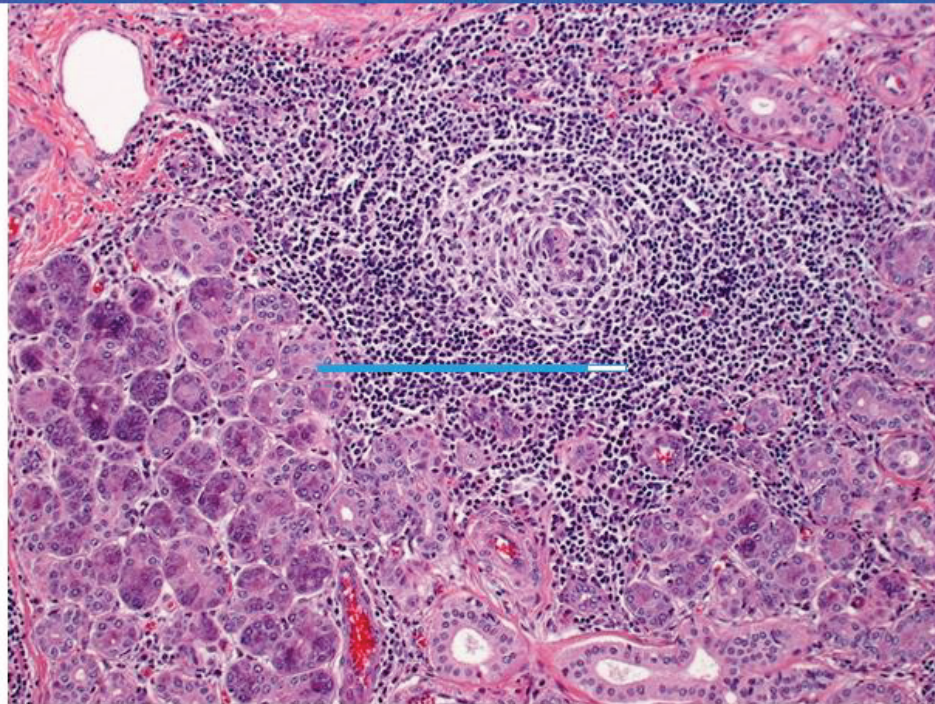
- ☐ A. Arterial and venous thrombosis
- ☐ B. Atlantoaxial subluxation
- ☐ C. Non-Hodgkin lymphoma
- ☐ D. Renal arterial occlusion
- ☐ E. Restrictive cardiomyopathy

and knee joints. The pain caused the patient to stop her daily yoga routine 2 months ago, and she has had difficulty performing daily household activities. She has had no fever, rash, or oral ulcers but frequently drinks water or chews gum due to her mouth feeling dry. The patient has no prior medical conditions and takes no medications or herbal supplements. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows no muscle tenderness or joint swelling. The thyroid gland is normal to palpation. There is nontender diffuse swelling of the parotid glands. Laboratory evaluation reveals mild normocytic normochromic anemia and an elevated erythrocyte sedimentation rate. A salivary gland biopsy image representative of this patient's disease process is shown in the [exhibit](#). This patient is at greatest risk for which of the following due to her current condition?

- ☐ A. Arterial and venous thrombosis
- ☐ B. Atlantoaxial subluxation
- ☐ C. Non-Hodgkin lymphoma
- ☐ D. Renal arterial occlusion
- ☐ E. Restrictive cardiomyopathy

and knee joints. The pain caused the patient to stop her daily yoga routine 2 months ago, and she has had

Exhibit Display



Zoom In

Zoom Out

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New | Existing

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drinks water or chews gum due to her **mouth feeling dry**. The patient has no prior medical conditions and takes no medications or herbal supplements. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination shows no muscle tenderness or joint swelling. The thyroid gland is normal to palpation. There is nontender **diffuse swelling** of the **parotid** glands. Laboratory evaluation reveals mild normocytic normochromic anemia and an elevated erythrocyte sedimentation rate. A salivary gland biopsy image representative of this patient's disease process is shown in the **exhibit**. This patient is at greatest risk for which of the following due to her current condition?

- ☐ A. Arterial and venous thrombosis (8%)
- ☐ B. Atlantoaxial subluxation (11%)
- ☒ C. Non-Hodgkin lymphoma (55%)
- ☐ D. Renal arterial occlusion (5%)
- ☐ E. Restrictive cardiomyopathy (19%)

Correct

55%



01 min, 14 secs



09/29/2020

Block Time Remaining: 00:20:41

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Feedback

Suspend

End Block

Sjögren syndrome

| | |
|--------------------------|---|
| Pathogenesis | <ul style="list-style-type: none">• Immune-mediated destruction of the lacrimal & salivary glands• Can occur as primary disease or secondary with other autoimmune disorders (eg, SLE, RA) |
| Clinical features | <ul style="list-style-type: none">• Dry eyes (keratoconjunctivitis sicca)• Dry mouth (xerostomia), salivary hypertrophy• Dry skin (xerosis)• Raynaud phenomenon• Cutaneous vasculitis• Positive anti-Ro (SSA) &/or anti-La (SSB) |
| Complications | <ul style="list-style-type: none">• Non-Hodgkin lymphoma• Corneal damage, dental caries |

RA = rheumatoid arthritis; **SLE** = systemic lupus erythematosus; **SSA/SSB** = Sjögren syndrome (antibody) A/B.

This patient with chronic dry mouth and palpable salivary gland enlargement has extensive **lymphocytic** infiltration with a germinal center on salivary gland biopsy, consistent with Sjögren syndrome (SS). SS is

RA = rheumatoid arthritis; **SLE** = systemic lupus erythematosus; **SSA/SSB** = Sjögren syndrome (antibody) A/B.

This patient with chronic dry mouth and palpable salivary gland enlargement has extensive **lymphocytic infiltrate** with a **germinal center** on salivary gland biopsy, consistent with **Sjögren syndrome** (SS). SS is an autoimmune disorder characterized by a lymphocytic inflammatory infiltrate in the **exocrine glands**. It presents with **dry eyes** (keratoconjunctivitis sicca) and **dry mouth** (xerostomia). Extraglandular manifestations such as **arthralgias** and cutaneous vasculitis can also occur due to deposition of circulating immune complexes.

Complications of SS can include corneal ulcerations (due to diminished lacrimal gland function) and an increase in dental caries (due to diminished salivary gland function). The chronic B-lymphocyte stimulation in SS also predisposes patients to malignant transformation, causing **non-Hodgkin lymphoma** (eg, marginal zone lymphoma, diffuse large B-cell lymphoma).

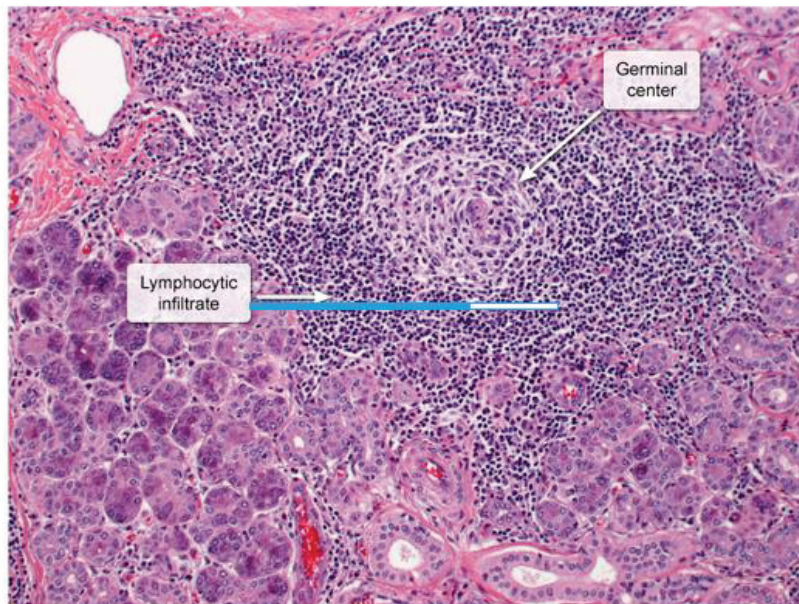
(Choice A) Systemic lupus erythematosus is associated with increased risk for arterial and venous thrombosis due to autoantibody production (antiphospholipid antibodies). Patients with this disease also often have arthralgias and anemia, but dry mouth and parotid enlargement in association with the characteristic biopsy findings are more characteristic of SS.

(Choice B) Atlantoaxial subluxation (ie, displacement of C1 on C2 vertebrae) is caused by ligamentous

RA = rheumatoid arthritis; SLE = systemic lupus erythematosus; SSA/SSB = Sjögren syndrome (antibody) A/B

Exhibit Display

Sjogren syndrome



Salivary gland excisional biopsy

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often have arthralgias and anemia, but dry mouth and parotid enlargement in association with the characteristic biopsy findings are more characteristic of SS.

(Choice B) Atlantoaxial subluxation (ie, displacement of C1 on C2 vertebrae) is caused by ligamentous deterioration in the cervical spine. It can be seen in a variety of inflammatory disorders (eg, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis) but is not common in SS.

(Choice D) Renal artery stenosis (occlusion) is most commonly seen in the context of advanced atherosclerosis or fibromuscular dysplasia and often causes treatment resistant hypertension.

(Choice E) Restrictive cardiomyopathy is often idiopathic or can be associated with infiltrative disorders (eg, amyloidosis, sarcoidosis, hemochromatosis). Cardiac manifestations of SS are rare and do not include restrictive disease.

Educational objective:

Sjögren syndrome (SS) is an autoimmune disorder characterized by lymphocytic inflammation in exocrine glands (eg, lacrimal, salivary glands). It presents with dry eyes (keratoconjunctivitis sicca) and dry mouth (xerostomia). Chronic B-cell proliferation in patients with SS increases the risk of developing non-Hodgkin lymphoma.

References



A 62-year-old woman comes to the office due to activity-related joint pain in the hands and periodic morning stiffness that lasts 10-15 minutes. The pain is moderately severe and has begun to limit her activities. The patient has attempted to treat the pain with acetaminophen, which provided only partial relief. Past medical history is notable for hypertension and diabetes mellitus. Physical examination shows firm nodules over the distal interphalangeal joints bilaterally as shown in the image below.



Exhibit Display



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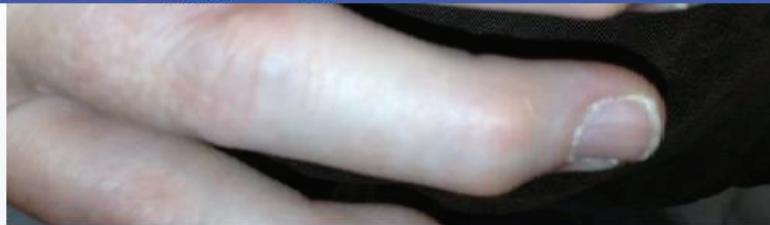
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Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Fibromyalgia
- ☐ B. Gout
- ☐ C. Infectious arthritis
- ☐ D. Osteoarthritis
- ☐ E. Reactive arthritis
- ☐ F. Rheumatoid arthritis



Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Fibromyalgia (0%)
- ☐ B. Gout (2%)
- ☐ C. Infectious arthritis (0%)
- ☒ D. Osteoarthritis (67%)
- ☐ E. Reactive arthritis (1%)
- ☐ F. Rheumatoid arthritis (27%)

Correct

67%



01 min, 19 secs



10/25/2020

Block Time Remaining: 00:22:00

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Feedback

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End Block

Osteoarthritis versus rheumatoid arthritis

| | Osteoarthritis | Rheumatoid arthritis |
|-----------------------------|--|--|
| Age of onset | >40; increases with age | 40-60; often younger |
| Joint involvement | <ul style="list-style-type: none">• Knees• Hips• DIP joint• 1st CMC joint | <ul style="list-style-type: none">• MCP joint• PIP joint• Wrists |
| Morning stiffness | None/brief (<30 min) | Prolonged |
| Systemic symptoms | Absent | <ul style="list-style-type: none">• Fever• Fatigue• Weight loss |
| Examination findings | <ul style="list-style-type: none">• Hard, bony enlargement of joints | <ul style="list-style-type: none">• Soft/spongy, warm joints |

CMC = carpometacarpal; DIP = distal interphalangeal; MCP = metacarpophalangeal;



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient, an older woman with use-dependent joint pain, has typical features of **osteoarthritis (OA)**. Patients with OA of the hands may also have osteophyte formation leading to bony enlargement of the **distal interphalangeal (DIP) and proximal interphalangeal (PIP)** joints (Heberden and Bouchard nodes, respectively). OA also commonly involves the spine and the large weight-bearing joints of the lower extremities (knees, hips). Morning stiffness is more typical of the inflammatory arthritides such as rheumatoid arthritis (RA), but may be experienced for a short duration (<30 minutes) in patients with OA as well.

In contrast, morning stiffness in RA may persist for hours and is often accompanied by systemic symptoms (eg, fever, weight loss). RA typically causes symmetric arthritis of the metacarpophalangeal, PIP, and other joints, but DIP joint involvement is less common (**Choice F**). In contrast to the bony enlargement in OA, the involved joints in RA have active synovitis, with warmth and spongy swelling.

(Choice A) Fibromyalgia is characterized by diffuse musculoskeletal pain that worsens with weather changes, psychological stress, or reduced sleep. It does not cause joint deformities.

(Choice B) Gout causes acute, episodic inflammatory monoarthritis that is characterized by a red, swollen, and painful joint. It usually affects the first metatarsophalangeal joint, knees, or ankles.

(Choice C) Septic arthritis causes intense pain, swelling, and redness of affected joints. The knee, hip,



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Feedback



Suspend



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(Choice A) Fibromyalgia is characterized by diffuse musculoskeletal pain that worsens with weather changes, psychological stress, or reduced sleep. It does not cause joint deformities.

(Choice B) Gout causes acute, episodic inflammatory monoarthritis that is characterized by a red, swollen, and painful joint. It usually affects the first metatarsophalangeal joint, knees, or ankles.

(Choice C) Septic arthritis causes intense pain, swelling, and redness of affected joints. The knee, hip, and shoulder are most commonly involved. The finger joints are less often affected and bony joint enlargement is not typical. Moreover, systemic signs, including fever, chills, and malaise, may be present.

(Choice E) Reactive arthritis is characterized by urethritis, conjunctivitis/uveitis, and arthritis (mainly of the knees, ankles, and feet) and is most common in young men. Hand joint involvement is not typical.

Educational objective:

Osteoarthritis of the hands is characterized by osteophyte formation leading to hard bony enlargement of the distal interphalangeal joints (Heberden nodes) and proximal interphalangeal joints (Bouchard nodes). Brief morning stiffness may be present.

References

- [EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT.](#)





A 27-year-old man comes to the emergency department due to severe left knee pain and swelling for the past 2 days. He has no recent injury or significant medical problems. The patient drinks 3 or 4 cans of beer daily but does not use tobacco or illicit drugs. He works as a groundskeeper at a nearby golf course and has had to take the last couple of days off because of the pain. Temperature is 38.3 C (101 F), blood pressure is 115/70 mm Hg, and pulse is 92/min. On examination, the left knee is swollen, erythematous, warm, and tender with restricted range of active and passive motion. The remainder of the examination is unremarkable. Which of the following is the best next step in management of this patient?

- ☐ A. Ibuprofen and follow up in 3 days
- ☐ B. MRI of the knee joint
- ☐ C. Radionuclide bone scan
- ☐ D. Serum uric acid level
- ☐ E. Synovial fluid analysis

Submit

A 27-year-old man comes to the emergency department due to severe left knee pain and swelling for the past 2 days. He has no recent injury or significant medical problems. The patient drinks 3 or 4 cans of beer daily but does not use tobacco or illicit drugs. He works as a groundskeeper at a nearby golf course and has had to take the last couple of days off because of the pain. Temperature is 38.3 C (101 F), blood pressure is 115/70 mm Hg, and pulse is 92/min. On examination, the left knee is swollen, erythematous, warm, and tender with restricted range of active and passive motion. The remainder of the examination is unremarkable. Which of the following is the best next step in management of this patient?

- ☒ A. Ibuprofen and follow up in 3 days (7%)
- ☐ B. MRI of the knee joint (3%)
- ☐ C. Radionuclide bone scan (0%)
- ☐ D. Serum uric acid level (10%)
- ☒ E. Synovial fluid analysis (78%)

Incorrect

Block Time Remaining: 00:25:09

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient has acute joint pain, swelling, and erythema with restricted range of motion, consistent with **synovitis**. Acute undiagnosed synovitis, especially when accompanied by fever or leukocytosis, represents a true emergency and warrants an expedited evaluation. Potential causes include septic arthritis (gonococcal, nongonococcal), crystal arthropathy (eg, gout), hemarthrosis, or rheumatic disease. Delayed diagnosis of septic arthritis may lead to loss of the joint and long-term disability, and may be fatal **(Choice A)**.

Acute synovitis is best evaluated with **diagnostic arthrocentesis** and synovial fluid analysis. Gross inspection may assist the diagnosis, with purulent or cloudy fluid suggesting an infectious or inflammatory process. Fluid should be sent for **crystal analysis, cell count, Gram stain, and culture**. Blood cultures should also be drawn if septic arthritis is suspected.

(Choice B) MRI is useful to evaluate menisci, ligaments, and other soft tissues around the joint. However, MRI can be time-consuming and would not provide a definitive diagnosis of septic arthritis.

(Choice C) Radionuclide bone scans are useful in the evaluation of metastatic and infectious bone disorders. However, the findings are sensitive but very nonspecific for potential causes of synovitis.

(Choice D) Synovial fluid crystal analysis is the definitive test for gout. Serum uric acid levels are less



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Feedback



Suspend



End Block

MRI can be time-consuming and would not provide a definitive diagnosis of septic arthritis.

(Choice C) Radionuclide bone scans are useful in the evaluation of metastatic and infectious bone disorders. However, the findings are sensitive but very nonspecific for potential causes of synovitis.

(Choice D) Synovial fluid crystal analysis is the definitive test for gout. Serum uric acid levels are less useful for diagnosis and may be normal during an acute gout attack. In addition, serum uric acid levels do not rule out other important causes of synovitis such as septic arthritis.

Educational objective:

Synovitis is characterized by pain, erythema, swelling, and reduced range of motion in a joint. Acute synovitis may represent serious pathology (eg, septic arthritis), especially if accompanied by fever or leukocytosis; it should be evaluated urgently with synovial fluid analysis.

References

- [Septic arthritis: current diagnostic and therapeutic algorithm.](#)

Pathology

Rheumatology/Orthopedics & Sports

Septic arthritis

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 46-year-old woman comes to the clinic to establish primary care as a new patient. She is a marathon runner but has been unable to train due to a vertebral stress fracture diagnosed via x-ray during a recent emergency department visit. She has a history of hypothyroidism for which she takes levothyroxine. The patient's last menstrual period was a year ago. Her diet consists mainly of vegetables and fruit, and she takes a daily multivitamin. Her mother died of breast cancer at age 52. The patient is concerned that her family history puts her at risk for breast cancer. X-ray absorptiometry studies demonstrate abnormally low bone density in the lumbar vertebrae. Which of the following drugs is the most appropriate option for decreasing the risk of both bone fractures and breast cancer in this patient?

- ☐ A. Alendronate
- ☐ B. Ethinyl estradiol
- ☐ C. Leuprolide
- ☐ D. Medroxyprogesterone
- ☐ E. Raloxifene
- ☐ F. Tamoxifen



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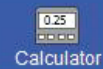
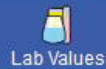
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runner but has been unable to train due to a vertebral stress fracture diagnosed via x-ray during a recent emergency department visit. She has a history of hypothyroidism for which she takes levothyroxine. The patient's last menstrual period was a year ago. Her diet consists mainly of vegetables and fruit, and she takes a daily multivitamin. Her mother died of breast cancer at age 52. The patient is concerned that her family history puts her at risk for breast cancer. X-ray absorptiometry studies demonstrate abnormally low bone density in the lumbar vertebrae. Which of the following drugs is the most appropriate option for decreasing the risk of both bone fractures and breast cancer in this patient?

- ☐ A. Alendronate (6%)
- ☐ B. Ethinyl estradiol (4%)
- ☐ C. Leuprolide (1%)
- ☐ D. Medroxyprogesterone (2%)
- ☒ E. Raloxifene (62%)
- ☐ F. Tamoxifen (22%)



Selective estrogen receptor modulators

| | |
|----------------------------|--|
| Drugs | <ul style="list-style-type: none">• Tamoxifen• Raloxifene |
| Mechanism of action | <ul style="list-style-type: none">• Competitive inhibitor of estrogen binding• Mixed agonist/antagonist action |
| Indications | <ul style="list-style-type: none">• Prevention of breast cancer in high-risk patients• Tamoxifen: adjuvant treatment of breast cancer• Raloxifene: postmenopausal osteoporosis |
| Adverse effects | <ul style="list-style-type: none">• Hot flashes• Venous thromboembolism• Endometrial hyperplasia & carcinoma (tamoxifen only) |

This patient has amenorrhea and low bone density, suggesting a low-estrogen state. This may be due to menopause, although her exercise history suggests possible hypothalamic amenorrhea (excessive exercise suppresses secretion of GnRH, leading to decreased release of FSH and low estrogen levels).



This patient has amenorrhea and low bone density, suggesting a low-estrogen state. This may be due to menopause, although her exercise history suggests possible hypothalamic amenorrhea (excessive exercise suppresses secretion of GnRH, leading to decreased release of FSH and low estrogen levels). Because estrogen decreases bone resorption, estrogen deficiency in women increases the risk for osteoporosis. Although estrogen replacement therapy (eg, ethinyl estradiol) can mitigate this risk, it can increase the risk of breast cancer and should be avoided in patients with a family history of breast cancer **(Choice B)**. In addition, unopposed estrogen (ie, without concurrent progesterone) can cause endometrial proliferation resulting in endometrial hyperplasia and cancer.

Selective estrogen receptor modulators (eg, raloxifene, tamoxifen) are nonsteroidal compounds that bind estrogen receptors and exhibit **antagonist and agonist** properties in a **tissue-specific** manner.

Raloxifene has estrogen agonist activity on bone, which decreases bone resorption, improves bone density, and decreases the risk of vertebral fractures. In addition, raloxifene has an estrogen antagonist effect on breast tissue and can decrease the risk of breast cancer. It also acts as an estrogen antagonist in the uterus and does not increase the risk of endometrial cancer.

Tamoxifen is a selective estrogen receptor modulator that has strong estrogen antagonist activity in the breast and is used in the treatment of estrogen receptor-positive breast cancer. It has estrogen-like effects



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Tamoxifen is a selective estrogen receptor modulator that has strong estrogen antagonist activity in the breast and is used in the treatment of estrogen receptor–positive breast cancer. It has estrogen-like effects on bone and can reduce the risk of osteoporosis in postmenopausal women. However, its agonist activity on the uterus increases the risk of endometrial hyperplasia/cancer and it is not appropriate for routine use in osteoporosis **(Choice F)**.

(Choice A) Bisphosphonates (eg, alendronate) inhibit osteoclast-mediated bone resorption. They have no estrogen agonist or antagonist activity and do not lower the risk of breast cancer.

(Choice C) Leuprolide is a GnRH analog that stimulates FSH and LH release (and subsequent estrogen production) when administered in a pulsatile manner (eg, via a programmable pump for treatment of anovulation) but suppresses release when administered continuously (eg, for endometriosis). Continuous use may reduce breast cancer risk but is associated with accelerated bone loss.

(Choice D) Medroxyprogesterone reduces the incidence of endometrial hyperplasia and endometrial carcinoma in postmenopausal women on estrogen replacement therapy, but otherwise has no benefit in management of osteoporosis. In addition, long-term use of medroxyprogesterone alone is associated with increased bone loss.

Educational objective:

Block Time Remaining: 00:25:31

TUTOR

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Feedback



Suspend



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(Choice A) Bisphosphonates (eg, alendronate) inhibit osteoclast-mediated bone resorption. They have no estrogen agonist or antagonist activity and do not lower the risk of breast cancer.

(Choice C) Leuprolide is a GnRH analog that stimulates FSH and LH release (and subsequent estrogen production) when administered in a pulsatile manner (eg, via a programmable pump for treatment of anovulation) but suppresses release when administered continuously (eg, for endometriosis). Continuous use may reduce breast cancer risk but is associated with accelerated bone loss.

(Choice D) Medroxyprogesterone reduces the incidence of endometrial hyperplasia and endometrial carcinoma in postmenopausal women on estrogen replacement therapy, but otherwise has no benefit in management of osteoporosis. In addition, long-term use of medroxyprogesterone alone is associated with increased bone loss.

Educational objective:

Selective estrogen receptor modulators exhibit estrogen antagonist and agonist properties in a tissue-specific manner. Raloxifene has estrogen agonist activity on bone, which decreases bone resorption and improves bone density. Raloxifene has an estrogen antagonist effect on breast tissue and can decrease the risk of breast cancer; it also acts as an estrogen antagonist in the uterus, and does not increase the risk of endometrial cancer.

References



A 43-year-old man comes to the office with muscle weakness. His symptoms began 6 weeks ago and are worst in the hips and shoulders. The weakness has had a progressive course so that he is now having difficulty rising from chairs and combing his hair. The patient has had to reduce his regular exercise regimen due to weakness and has requested a modified work schedule for his job as a building maintenance manager. He has no history of spinal injury and no neck pain. Past medical history is insignificant, and the patient takes no medications. Muscle biopsy reveals major histocompatibility complex class I molecule overexpression on the sarcolemma with CD8⁺ lymphocyte infiltration. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Diffuse systemic sclerosis
- ☐ B. Eaton-Lambert syndrome
- ☐ C. Myasthenia gravis
- ☐ D. Polyarteritis nodosa
- ☐ E. Polymyalgia rheumatica
- ☐ F. Polymyositis





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

difficulty rising from chairs and combing his hair. The patient has had to reduce his regular exercise regimen due to weakness and has requested a modified work schedule for his job as a building maintenance manager. He has no history of spinal injury and no neck pain. Past medical history is insignificant, and the patient takes no medications. Muscle biopsy reveals major histocompatibility complex class I molecule overexpression on the sarcolemma with CD8⁺ lymphocyte infiltration. Which of the following is the most likely cause of this patient's condition?

- ☐ A. Diffuse systemic sclerosis (1%)
- ☐ B. ~~Eaton-Lambert syndrome (7%)~~
- ☐ C. ~~Myasthenia gravis (4%)~~
- ☐ D. ~~Polyarteritis nodosa (0%)~~
- ☐ E. ~~Polymyalgia rheumatica (10%)~~
- ✓ ☒ F. Polymyositis (75%)

Correct

75%



01 min, 55 secs



11/01/2020

Block Time Remaining: 00:27:27

TUTOR

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1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Polymyositis

| | |
|---------------------------------|---|
| Clinical presentation | <ul style="list-style-type: none">• Symmetrical proximal muscle weakness• Increasing difficulty climbing stairs, getting up from a chair, carrying heavy objects |
| Pathologic features | <ul style="list-style-type: none">• Elevated muscle enzymes (CK, aldolase)• Autoantibodies (ANA, anti-Jo-1)• Biopsy: Endomysial mononuclear infiltrate, patchy necrosis |
| Associated complications | <ul style="list-style-type: none">• Interstitial lung disease• Myocarditis |

ANA = antinuclear antibodies; **CK** = creatine kinase.

This patient, a middle-aged man with progressive, symmetric **proximal muscle weakness**, has typical symptoms of **polymyositis**. The weakness may be painless or associated with diffuse myalgias. Muscle enzyme levels (eg, creatine kinase) are invariably elevated, and autoantibodies (eg, antinuclear antibodies, anti-Jo-1 antibodies) are present in most cases. Polymyositis is similar to dermatomyositis, although it



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

anti-Jo-1 antibodies) are present in most cases. Polymyositis is similar to dermatomyositis, although it lacks the typical **skin findings**; both may occur independently or as a paraneoplastic manifestation of an underlying malignancy.

Polymyositis is an inflammatory myopathy triggered by unknown, possibly viral, antigens. It likely represents a cell-mediated immune response against myocytes. Increased expression of **major histocompatibility complex class I** antigens on the sarcolemma has been demonstrated and likely leads to presentation of autoantigens to **CD8⁺ cytotoxic cells** that subsequently initiate myocyte destruction.

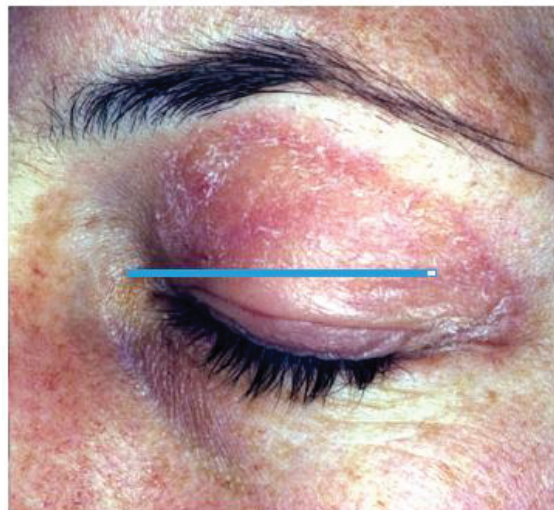
Muscle biopsy in polymyositis reveals inflammation, patchy necrosis, and regeneration and fibrosis of muscle fibers. Infiltration of the endomysium by macrophages and CD8⁺ lymphocytes is typically seen.

(Choice A) Joint involvement in systemic sclerosis may cause arthralgias and contractures, but muscle weakness is not seen.

(Choices B and C) Myasthenia gravis is caused by anti-acetylcholine receptor autoantibodies and is characterized by episodic weakness that initially affects the ocular/bulbar musculature. The Eaton-Lambert myasthenic syndrome is a paraneoplastic condition causing fatigable weakness in the extremities; it is caused by autoantibodies to presynaptic calcium channels. Light microscopy of muscle biopsy specimens is normal in these conditions.



Exhibit Display





myasthenic syndrome is a paraneoplastic condition causing fatigable weakness in the extremities; it is caused by autoantibodies to presynaptic calcium channels. Light microscopy of muscle biopsy specimens is normal in these conditions.

(Choice D) Polyarteritis nodosa is an uncommon systemic vasculitis that presents with intermittent episodes of abdominal pain, peripheral neuropathy, renal insufficiency, and severe hypertension. Biopsy is characterized by transmural inflammation of the arterial wall with fibrinoid necrosis.

(Choice E) Polymyalgia rheumatica (PMR) causes myalgias of the shoulder and pelvic girdle muscles, often with systemic symptoms (eg, fever, weight loss). Weakness is not typical, and PMR occurs almost exclusively in patients age >50.

Educational objective:

Polymyositis causes symmetric proximal muscle weakness. Muscle biopsy reveals inflammation, necrosis, and regeneration of muscle fibers. Over-expression of major histocompatibility complex class I proteins on the sarcolemma leads to infiltration with CD8⁺ T lymphocytes and myocyte damage.

References

- [Mechanisms of disease: signaling pathways and immunobiology of inflammatory myopathies.](#)





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 13-year-old boy comes to the office for evaluation of worsening scoliosis. He lost the ability to walk a year ago and has since been wheelchair bound. He has significant back pain and difficulty sitting in his wheelchair for extended periods. The patient also feels "too weak" to cough or take a deep breath. Review of medical records shows genetic studies confirming a mutation of the dystrophin gene on X chromosome p21. Histopathology of the patient's calf most likely indicates which of the following findings?

- ☐ A. Fibrofatty muscle replacement
- ☐ B. Hypertrophic muscle fibers
- ☐ C. Multiple lipid droplets within muscle fibers
- ☐ D. Prominent inflammatory infiltrate
- ☐ E. Ragged red fibers

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0



Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

A 13-year-old boy comes to the office for evaluation of worsening **scoliosis**. He lost the ability to walk a year ago and has since been **wheelchair** bound. He has significant back pain and difficulty sitting in his wheelchair for extended periods. The patient also feels "too weak" to cough or take a deep breath. Review of medical records shows **genetic studies** confirming a mutation of the **dystrophin** gene on X chromosome p21. Histopathology of the patient's calf most likely indicates which of the following findings?

- ✓ ☒ A. Fibrofatty muscle replacement (85%)
- ☐ B. Hypertrophic muscle fibers (6%)
- ☐ C. Multiple lipid droplets within muscle fibers (3%)
- ☐ D. Prominent inflammatory infiltrate (0%)
- ☐ E. Ragged red fibers (3%)

Correct

 85%
Answered correctly 40 secs
Time Spent 01/18/2021
Last Updated

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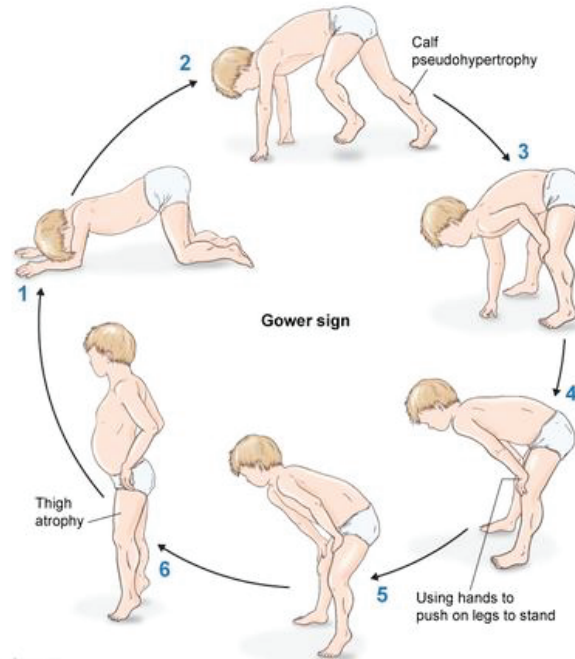


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New | Existing

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Deletion of the dystrophin gene causes Duchenne muscle dystrophy (DMD). The condition is **X-linked recessive** and therefore affects primarily **boys**. Dystrophin is a structural protein of muscle fibers, and its absence causes muscle fiber destruction (myonecrosis). Variation in muscle fiber shape and size, regenerating fibers, and increased amounts of connective tissue are seen on light microscopy.

Disease onset is age 2-5. Muscles of the proximal lower extremities, back, and pelvic and shoulder girdles are affected first. Symptoms of DMD include the following:

1. Ambulation difficulties: Clumsy, slow, waddling gait; cannot keep up with peers
2. Gower sign: Progressive weakness in proximal musculature, resulting in use of the hands to support weight on standing (as shown in the image above)
3. Calf **pseudohypertrophy**: Calf muscles hypertrophy initially in response to proximal muscle weakness and are later replaced by fat and connective tissue
4. Asymmetric weakening of the paraspinal muscles, leading to **kyphoscoliosis**

Most patients with DMD are **wheelchair bound by age 12**. Scoliosis progresses rapidly due to muscle imbalance and body positional changes. Worsening scoliosis is complicated by restrictive pulmonary function (decreased vital capacity and total lung capacity).

(Choice B) Hypertrophy of muscle fibers may occur in the early stages of DMD. However, fibrofatty





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) Hypertrophy of muscle fibers may occur in the early stages of DMD. However, fibrofatty change of the enlarged muscles would be expected in a patient at this advanced stage of the disease.

(Choice C) Lipid accumulation within muscle fibers is seen in lipid myopathies such as carnitine palmitoyltransferase deficiency.

(Choice D) Prominent inflammatory infiltrate is a characteristic histologic feature of polymyositis and dermatomyositis. These conditions cause proximal muscle weakness without distal pseudohypertrophy.

(Choice E) Ragged red fibers refer to muscle fibers with irregular contours and a blotchy red appearance. They are seen in mitochondrial myopathies.

Educational objective:

Duchenne muscle dystrophy manifests with proximal muscle weakness and atrophy. True hypertrophy of the distal muscle is noted early in the disease as distal muscles compensate for weak proximal ones.

Muscle fibers of the distal extremities are later replaced by fat and connective tissue (pseudohypertrophy).

References

- [Muscle disease.](#)
- [Entries in the Leiden Duchenne muscular dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading frame rule](#)



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 47-year-old woman comes to the physician with progressive joint pain and swelling in her hands for the past several months. She also has easy fatigability that has gradually worsened over the same period. Morning activities are especially difficult due to stiffness lasting 1 to 2 hours after waking. Examination shows warmth, swelling, and tenderness involving the proximal interphalangeal joints, metacarpophalangeal joints, and wrists bilaterally. A blood sample is obtained for laboratory analysis. Autoantibodies against which of the following components are most specific for this patient's condition?

- ☐ A. Centromeres
- ☐ B. Citrullinated peptides
- ☐ C. Double-stranded DNA
- ☐ D. Fc portion of human IgG
- ☐ E. Nuclear basic proteins
- ☐ F. Phospholipids

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Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 47-year-old woman comes to the physician with progressive joint pain and swelling in her hands for the past several months. She also has easy fatigability that has gradually worsened over the same period. Morning activities are especially difficult due to stiffness lasting 1 to 2 hours after waking. Examination shows warmth, swelling, and tenderness involving the proximal interphalangeal joints, metacarpophalangeal joints, and wrists bilaterally. A blood sample is obtained for laboratory analysis. Autoantibodies against which of the following components are most specific for this patient's condition?

- ☐ A. Centromeres (2%)
- ☒ B. Citrullinated peptides (52%)
- ☐ C. Double-stranded DNA (6%)
- ☐ D. Fc portion of human IgG (34%)
- ☐ E. Nuclear basic proteins (2%)
- ☐ F. Phospholipids (1%)



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Feedback



Suspend



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Clinical features of rheumatoid arthritis

| | |
|-----------------------------------|--|
| Clinical presentation | <ul style="list-style-type: none">• Pain, swelling & morning stiffness in multiple joints• Small joints (PIP, MCP, MTP); spares DIP joints• Systemic symptoms (fever, weight loss, anemia)• Cervical spine involvement: subluxation, cord compression |
| Laboratory/imaging studies | <ul style="list-style-type: none">• Positive rheumatoid factor & anti-CCP antibodies• C-reactive protein & ESR correlate with disease activity• X-ray: soft tissue swelling, joint space narrowing, bony erosions |

Anti-CCP = anti-cyclic citrullinated peptide; **DIP** = distal interphalangeal; **ESR** = erythrocyte sedimentation rate; **MCP** = metacarpophalangeal; **MTP** = metatarsophalangeal; **PIP** = proximal interphalangeal.

This patient's symmetric polyarthritis (involving the MCP and PIP joints) with prolonged morning stiffness and associated fatigue is highly suggestive of **rheumatoid arthritis** (RA). The diagnosis is made clinically,

This patient's symmetric polyarthritis (involving the MCP and PIP joints) with prolonged morning stiffness and associated fatigue is highly suggestive of **rheumatoid arthritis** (RA). The diagnosis is made clinically, but the presence of **anti-cyclic citrullinated peptide (anti-CCP) antibodies** is helpful for confirmation.

Tissue inflammation causes **arginine** residues in proteins such as vimentin to be enzymatically converted into **citrulline** through a process called citrullination. This alters the shape of the proteins, which can then serve as neoantigens that generate an immune response. In RA, the immune response against citrullinated proteins is exaggerated, resulting in high titers of anti-CCP antibodies that are not usually present in other inflammatory conditions. Thus, anti-CCP antibodies have a **high specificity** for RA. Antibodies to citrullinated peptides/proteins are usually measured by enzyme-linked immunosorbent assay (ELISA) using a mixture of CCPs as the antigen.

(Choice A) Anticentromere antibodies are found in the majority of patients with **CREST syndrome**.

(Choice C) Antibodies to double-stranded DNA (anti-dsDNA) are specific for systemic lupus erythematosus.

(Choice D) Rheumatoid factors are autoantibodies targeting the Fc portion of human IgG that occur in most patients with RA. Their diagnostic utility is limited by their **poor specificity** as they are found in

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CREST syndrome characteristics

Calcinosis
Raynaud phenomenon
Esophageal dysmotility
Sclerodactyly
Telangiectasias

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New | Existing

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(Choice D) Rheumatoid factors are autoantibodies targeting the Fc portion of human IgG that occur in most patients with RA. Their diagnostic utility is limited by their **poor specificity** as they are found in approximately 10% of healthy individuals, in 30% of patients with systemic lupus erythematosus, and in nearly all patients with mixed cryoglobulinemia.

(Choice E) The presence of antinuclear antibodies (ANA) is a nonspecific finding in many connective tissue disorders. Antinuclear antibodies characteristically occur in IgM form in patients with RA, but they are found less frequently than rheumatoid factors.

(Choice F) Antiphospholipid antibodies are found in patients with systemic lupus erythematosus and antiphospholipid antibody syndrome. Antiphospholipid antibody syndrome causes hypercoagulability, paradoxical partial thromboplastin time (PTT) prolongation, and recurrent miscarriages (spontaneous abortions).

Educational objective:

Rheumatoid arthritis is characterized by symmetric polyarthritis (involving the metacarpophalangeal and proximal interphalangeal joints) with prolonged morning stiffness and associated fatigue. Antibodies to citrullinated peptides/proteins have a high specificity for the condition.





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 10-year-old boy is brought to the emergency department after experiencing high fevers and chills for the last few days. He also complains of dull pain just above his left knee. He has no history of recent trauma other than minor scrapes to his knees and elbows while playing outside. Physical examination shows point tenderness 3 cm above the kneecap. There is no joint effusion. Radiographs show soft-tissue swelling and a periosteal reaction over the lower end of the femur. Which of the following organisms is most likely responsible for this patient's symptoms?

- ☐ A. *Enterococcus faecalis*
- ☐ B. *Moraxella catarrhalis*
- ☐ C. *Staphylococcus aureus*
- ☐ D. *Staphylococcus epidermidis*
- ☐ E. *Streptococcus agalactiae*
- ☐ F. *Streptococcus pneumoniae*
- ☐ G. *Streptococcus pyogenes*



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Feedback



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last few days. He also complains of dull pain just above his left knee. He has no history of recent trauma other than **minor scrapes** to his knees and elbows while playing outside. Physical examination shows point tenderness 3 cm above the kneecap. There is no joint effusion. Radiographs show soft-tissue swelling and a periosteal reaction over the lower end of the femur. Which of the following organisms is most likely responsible for this patient's symptoms?

- ☐ A. *Enterococcus faecalis* (0%)
- ☐ B. *Moraxella catarrhalis* (1%)
- ☒ C. *Staphylococcus aureus* (84%)
- ☐ D. *Staphylococcus epidermidis* (4%)
- ☐ E. *Streptococcus agalactiae* (0%)
- ☐ F. *Streptococcus pneumoniae* (1%)
- ☐ G. *Streptococcus pyogenes* (6%)

Correct

84%



55 secs



12/29/2020

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Feedback



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Causes of osteomyelitis

| Associated condition | Mode of infection | Most frequent pathogen | Typical location |
|---|--|---|-------------------|
| Childhood age | Hematogenous seeding during an episode of bacteremia | <i>Staphylococcus aureus</i> | Long bones |
| Sickle cell disease | Hematogenous seeding to infarcted bone | <i>Salmonella</i> <i>Staphylococcus aureus</i> | Long bones |
| Pott disease | Hematogenous seeding from lungs | <i>Mycobacterium tuberculosis</i> | Vertebrae |
| Diabetes mellitus | Contiguous spread from infected foot ulcer | Polymicrobial | Bones of the feet |
| Recumbent patients with impaired mobility | Contiguous spread from pressure sores | Polymicrobial | Sacrum & heels |



0



Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

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| Recent trauma or orthopedic surgery | Direct inoculation | Polymicrobial | Variable |
|-------------------------------------|--------------------|---------------|----------|

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Osteomyelitis is an infection of bone and bone marrow that occurs by 1 of 3 mechanisms:

1. Hematogenous seeding due to an episode of bacteremia
2. Spread from a contiguous focus of infection, as occurs in an infected diabetic foot wound
3. Direct inoculation of bone, such as with a compound fracture

Hematogenous osteomyelitis occurs predominantly in children (particularly boys) and most frequently affects the long bones. The tibia, fibula, and femur are most often involved. Adults who develop the condition are more likely to have vertebral involvement and frequently have a predisposition to bacteremia due to risk factors such as IV drug abuse or indwelling vascular catheters.

The presenting symptoms of hematogenous osteomyelitis are vague, and a high index of suspicion is required to make the diagnosis. Initial symptoms such as malaise and fevers are non-specific. As the infection progresses, infants and younger children may refuse to move the affected extremity. Older children often complain of pain over a long bone. Bone pain develops as the abscess expands within the bone, leading to bone necrosis, periosteal disruption, and swelling of the surrounding soft tissue.



0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

infection progresses, infants and younger children may refuse to move the affected extremity. Older children often complain of pain over a long bone. Bone pain develops as the abscess expands within the bone, leading to bone necrosis, periosteal disruption, and swelling of the surrounding soft tissue.

Staphylococcus aureus is implicated in most cases of acute hematogenous osteomyelitis in otherwise healthy children.

(Choice A) *Enterococcus faecalis* causes a variety of infections, including endocarditis, meningitis, and urinary tract infections. *Enterococcus* can cause vertebral osteomyelitis after a recent urinary tract infection via bacteremic spread.

(Choice B) *Moraxella catarrhalis* is a part of the normal flora of the upper respiratory tract. It causes otitis media and sinusitis in healthy individuals and is frequently responsible for causing exacerbation of chronic obstructive pulmonary disease.

(Choice D) *Staphylococcus epidermidis* is ubiquitous in nature and is commonly isolated in cultures as a contaminant. However, *S epidermidis* can also be pathogenic, colonizing intravenous catheters and other foreign bodies such as prosthetic heart valves and orthopedic hardware, leading to bacteremia and sepsis.

(Choice E) *Streptococcus agalactiae* (group B streptococcus) frequently colonizes the gastrointestinal and urogenital tracts. Infants born vaginally to colonized mothers can develop serious neonatal infections.



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

foreign bodies such as prosthetic heart valves and orthopedic hardware, leading to bacteremia and sepsis.

(Choice E) *Streptococcus agalactiae* (group B streptococcus) frequently colonizes the gastrointestinal and urogenital tracts. Infants born vaginally to colonized mothers can develop serious neonatal infections, including sepsis, pneumonia, and meningitis. For this reason, pregnant women testing positive for group B streptococci are treated with antibiotic prophylaxis during labor and delivery.

(Choice F) *Streptococcus pneumoniae* is the most common etiologic agent of community-acquired pneumonia. It also causes otitis media in children, sinusitis, meningitis, and sepsis.

(Choice G) After *Staphylococcus aureus*, *Streptococcus pyogenes* (group A streptococcus) is the second most common cause of hematogenous osteomyelitis in children. Group A streptococci are also responsible for streptococcal pharyngitis and skin infections such as impetigo and necrotizing fasciitis.

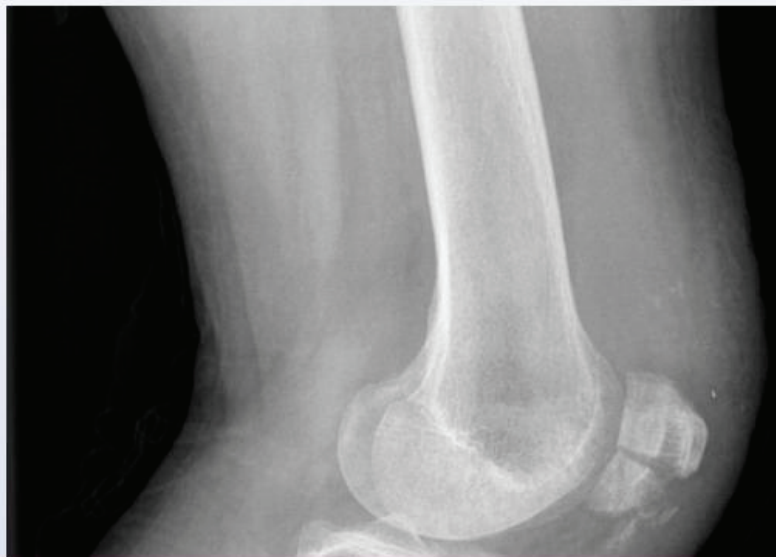
Educational objective:

Hematogenous osteomyelitis is predominantly a disease of children that most frequently affects the long bones. *Staphylococcus aureus* is implicated in most cases secondary to a bacteremic event.

Streptococcus pyogenes (group A streptococcus) is the second most common cause of hematogenous osteomyelitis.



A 46-year-old woman is brought by ambulance to the emergency department following a ground-level fall at home. She slipped while getting out of the shower and hit her left knee on the tile floor. The patient developed severe left knee pain and swelling and is unable to ambulate. Examination shows a contusion and soft tissue swelling at the knee with a large knee effusion. X-ray of the knee is shown in the image below:





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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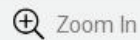


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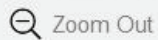


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0



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Which of the following examination findings would most likely be seen in this patient?

- ☐ A. Backward movement of the tibia against a fixed femur
- ☐ B. Excessive joint widening on valgus stress
- ☐ C. Forward movement of the tibia against a fixed femur
- ☐ D. Inability to extend the knee against gravity
- ☐ E. Inability to flex the knee against resistance

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Feedback



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End Block



Which of the following examination findings would most likely be seen in this patient?

- ☐ A. Backward movement of the tibia against a fixed femur (2%)
- ☐ B. Excessive joint widening on valgus stress (1%)
- ☐ C. Forward movement of the tibia against a fixed femur (6%)
- ☒ D. Inability to extend the knee against gravity (79%)
- ☐ E. Inability to flex the knee against resistance (9%)

Correct

79%

27 secs

12/05/2020

Block Time Remaining: 00:30:27

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



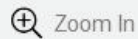
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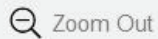
Patellar fracture



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0



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This patient has a comminuted **patella fracture**. The patella is a large sesamoid bone that facilitates knee extension, protects the joint from direct injury, and improves nourishment of the distal femur articular cartilage. The quadriceps tendon inserts at the superior pole of the patella and wraps distally around the patella to become the patellar tendon, which inserts at the tibial tuberosity.

Patella fractures are most commonly due to a **direct blow** to the **anterior aspect** of the knee (eg, landing on a flexed knee in a fall, striking the knee against the dashboard in a frontal motor vehicle collision). The patella can also be fractured indirectly due to excessive force transmitted through the quadriceps tendon (eg, landing on the feet after falling from a height). Patients develop acute swelling (often with an associated effusion), focal tenderness, **inability to extend the knee** against gravity, and a **palpable gap** in the extensor mechanism.

(Choice A) The posterior cruciate ligament (PCL) protects against excessive posterior knee movement and is the least frequently injured knee ligament. PCL injury results in a positive posterior drawer test (increased backward movement of the tibia against a fixed femur).

(Choice B) The medial collateral ligament (MCL) protects against valgus stress on the knee and excessive external tibial rotation. MCL injury occurs after a **lateral blow to the knee** or indirect stress from excessive

(increased backward movement of the tibia against a fixed femur).

(Choice B) The medial collateral ligament (MCL) protects against valgus stress on the knee and excessive external tibial rotation. MCL injury occurs after a **lateral blow to the knee** or indirect stress from excessive lower leg rotation or abduction. Patients have excessive joint widening on valgus stress (eg, the femur is held in a fixed position while an abducting [lateral] force is applied to the lower leg/foot).

(Choice C) The anterior cruciate ligament (ACL) controls anterior knee movement and prevents excessive tibial rotation. ACL injury often occurs due to sudden acceleration or deceleration in noncontact athletic injuries. Patients have laxity of forward movement of the tibia against a fixed femur (**anterior drawer test**).

(Choice E) Knee flexors include the hamstring muscles (biceps femoris, semitendinosus, semimembranosus), gracilis, gastrocnemius, and sartorius. Hamstring injury can decrease hip extension and knee flexion. However, these muscles do not involve the patella.

Educational objective:

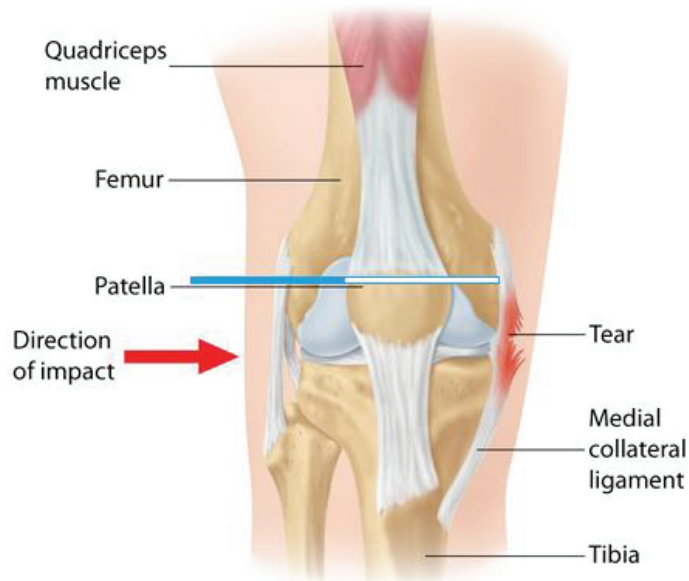
Patella fractures are most commonly due to a direct impact to the anterior aspect of the knee. Signs include an acutely swollen knee, focal patella tenderness, inability to extend the knee against gravity, and a palpable gap in the extensor mechanism.

References

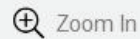
(increased backward movement of the tibia against a fixed femur)

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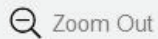
Medial collateral ligament injury



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0



Feedback



Suspend



End Block

(increased backward movement of the tibia against a fixed femur)

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Tests for anterior cruciate ligament tear

Anterior drawer test



Lachman test



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Zoom Out

Reset

New | Existing

My Notebook

References

Block Time Remaining: 00:30:27

TUTOR

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

An 18-month-old boy is brought to the office by his mother for a well-child visit. The family recently immigrated to the United States from Nigeria. The patient was born full term and is up to date with vaccinations. He was exclusively breastfed until age 5 months and has since had a varied diet of fruits, vegetables, and meats with continued breastfeeding. The patient started walking a month ago and says 10-15 words. He takes no medications or supplements. Physical examination reveals frontal bossing and bilateral tibial and femoral bowing. Which of the following abnormalities is most likely seen in this patient?

- ☐ A. Deficiency of type I collagen
- ☐ B. Excess of mineralized matrix
- ☐ C. Excess of osteoclast activity
- ☐ D. Excess of unmineralized matrix
- ☐ E. Inhibition of cartilaginous growth

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Text Zoom



Settings

An 18-month-old boy is brought to the office by his mother for a well-child visit. The family recently immigrated to the United States from Nigeria. The patient was born full term and is up to date with vaccinations. He was exclusively breastfed until age 5 months and has since had a varied diet of fruits, vegetables, and meats with continued breastfeeding. The patient started walking a month ago and says 10-15 words. He takes no medications or supplements. Physical examination reveals frontal bossing and bilateral tibial and femoral bowing. Which of the following abnormalities is most likely seen in this patient?

- ☐ A. Deficiency of type I collagen (9%)
- ☐ B. Excess of mineralized matrix (3%)
- ☐ C. Excess of osteoclast activity (6%)
- ☒ D. Excess of unmineralized matrix (72%)
- ☐ E. Inhibition of cartilaginous growth (7%)

Correct

 72%
Answered correctly 01 min, 46 secs
Time Spent 02/26/2021
Last Updated

Block Time Remaining: 00:32:13

TUTOR

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Nutritional rickets in children

Risk factors

- Exclusive breastfeeding
- Inadequate sun exposure
- Increased skin pigmentation
- Maternal vitamin D deficiency

Clinical manifestations

- Craniotabes ("ping-pong ball" skull)
- Widening of wrists
- Delayed fontanel closure
- Frontal bossing
- Hypertrophy of costochondral joints ("rachitic rosary")
- Femoral & tibial bowing once weight-bearing

Evaluation

- Serum calcium; phosphorus; alkaline phosphatase; parathyroid hormone; 25-hydroxyvitamin D;



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

| | |
|-------------------|--|
| | <ul style="list-style-type: none">• Femoral & tibial bowing once weight-bearing |
| Evaluation | <ul style="list-style-type: none">• Serum calcium; phosphorus; alkaline phosphatase; parathyroid hormone; 25-hydroxyvitamin D; 1,25-dihydroxyvitamin D• Radiography |
| Management | <ul style="list-style-type: none">• Vitamin D & calcium supplementation |

Vitamin D is essential for calcium and phosphorus homeostasis and can be endogenously produced with subsequent metabolization through ultraviolet B light exposure and/or exogenously supplemented through diet/vitamins. **Insufficient vitamin D** levels result from decreased conversion to the active form (eg, increased skin pigmentation, limited sun exposure) and/or inadequate intake (eg, exclusive breastfeeding). Low vitamin D leads to hypocalcemia and/or hypophosphatemia due to reduced intestinal absorption of these minerals. Parathyroid hormone secretion is markedly elevated to mobilize calcium from bone to the bloodstream in an attempt to maintain serum calcium levels. Inadequate calcium and phosphorus for the



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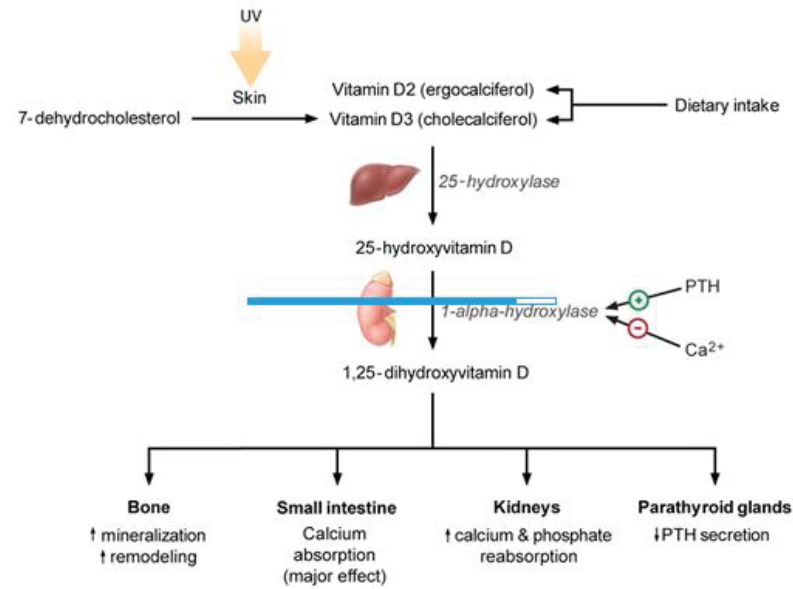


End Block

Femoral & tibial bowing once

Exhibit Display

Normal vitamin D metabolism



PTH = parathyroid hormone.
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bone leads to **rickets**, which is characterized by an excess of **unmineralized osteoid matrix** and epiphyseal (growth plate) cartilage.

Clinical manifestations vary with age. Prior to ambulation, **frontal bossing**, **craniotabes** (softened skull bones), and costochondral junction widening from cartilage overgrowth ("rachitic rosary") are apparent. Once weight bearing, which may be delayed due to decreased muscle tone, patients have lateral femoral and tibial bowing (**genu varum**). Radiograph of growth plates (eg, distal ulna) will reveal **metaphyseal plate widening and cupping**.

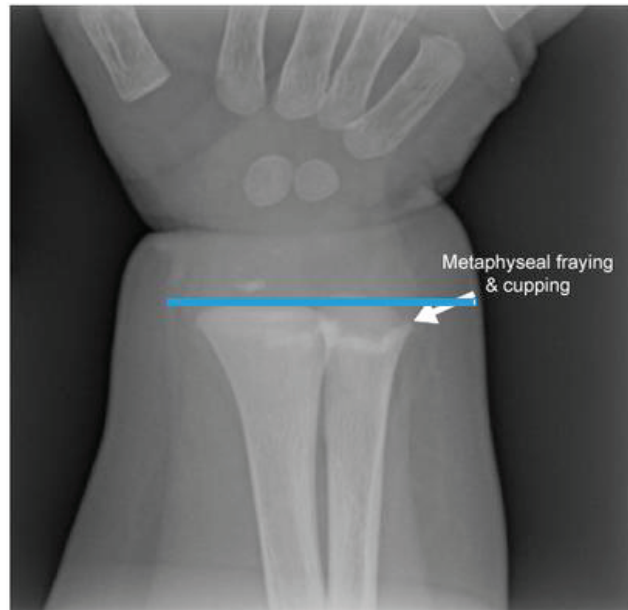
(Choice A) Osteogenesis imperfecta is caused by ~~type I collagen deficiency~~ resulting in bone fragility and frequent fractures, blue sclerae, and hearing loss.

(Choice B) Osteosarcoma is the most common malignant bone tumor in children and is characterized by excessive production of mineralized bone. The enlarging mass may lift the periosteum and extend into surrounding soft tissues.

(Choice C) Paget disease is seen in patients age >55 who may be asymptomatic or have focal bone pain, fractures, and/or deformity (eg, anterior femoral and tibial bowing). Excess osteoclastic activity followed by new bone formation results in disordered bone mass, which appears histologically as a haphazard arrangement of lamellar bone.

Exhibit Display

Rickets



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Previous



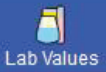
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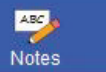
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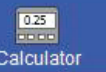
Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

fractures, and/or deformity (eg, anterior femoral and tibial bowing). Excess osteoclastic activity followed by new bone formation results in disordered bone mass, which appears histologically as a haphazard arrangement of lamellar bone.

(Choice E) [Achondroplasia](#) is an autosomal dominant disorder characterized by an exaggerated inhibition of cartilage proliferation. Clinical manifestations include short stature with proximal limb shortening, frontal bossing, and midface hypoplasia.

Educational objective:

Rickets is characterized by an excess of unmineralized osteoid matrix and epiphyseal cartilage due to vitamin D deficiency. Clinical manifestations include frontal bossing, craniotabes, costochondral junction deformity ("rachitic rosary"), and bowed legs.

References

- [Nutritional rickets around the world.](#)
- [Rickets: part I.](#)

Pathology

Rheumatology/Orthopedics & Sports

Vitamin D deficiency

Subject

System

Topic

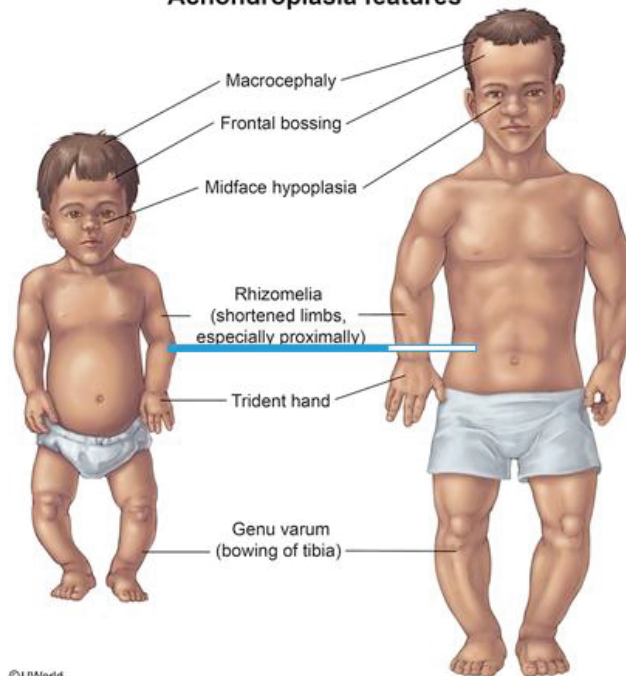
Block Time Remaining: 00:32:13

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Exhibit Display

Achondroplasia features



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Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 76-year-old man comes to the office with a 2-month history of progressive low back pain. The pain is relatively constant and nagging and is unrelieved by rest or position changes. It is especially bad at night and interferes with sleep. The patient has taken acetaminophen and ibuprofen without relief. Medical history is significant for hypertension and osteoarthritis affecting the knees and hands. The patient used intravenous drugs occasionally when he was younger but not for >30 years. Which of the following processes is most likely responsible for this patient's back pain?

- ☐ A. Degenerative
- ☐ B. Infectious
- ☐ C. Inflammatory
- ☐ D. Neoplastic
- ☐ E. Psychogenic

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



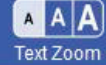
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 76-year-old man comes to the office with a 2-month history of progressive low back pain. The pain is relatively constant and nagging and is unrelieved by rest or position changes. It is especially bad at night and interferes with sleep. The patient has taken acetaminophen and ibuprofen without relief. Medical history is significant for hypertension and osteoarthritis affecting the knees and hands. The patient used intravenous drugs occasionally when he was younger but not for >30 years. Which of the following processes is most likely responsible for this patient's back pain?

- ☐ A. Degenerative (36%)
- ☐ B. Infectious (3%)
- ☐ C. Inflammatory (4%)
- ☒ D. Neoplastic (55%)
- ☐ E. Psychogenic (0%)

Correct

55%
Answered correctly
01 min, 04 secs
Time Spent
09/24/2020
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Block Time Remaining: 00:33:18

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Differential diagnosis of back pain

| Condition | Clinical clues |
|---|---|
| Degenerative (osteoarthritis) | <ul style="list-style-type: none">• Positional• Relieved with rest |
| Radiculopathy (eg, disc herniation) | <ul style="list-style-type: none">• Radiates to leg• Sensory & motor findings• Positive straight-leg raising test |
| Spinal stenosis | <ul style="list-style-type: none">• Pain with standing (spinal extension)• Relieved by spinal flexion |
| Spondyloarthropathy | <ul style="list-style-type: none">• Young men• HLA-B27• Relieved with exercise• Prolonged morning stiffness |
| Spinal metastasis | <ul style="list-style-type: none">• Constant pain• Worse at night |



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

| | |
|--------------------------------|---|
| | <ul style="list-style-type: none">• Prolonged morning stiffness |
| Spinal metastasis | <ul style="list-style-type: none">• Constant pain• Worse at night• Not responsive to position changes |
| Vertebral osteomyelitis | <ul style="list-style-type: none">• Focal tenderness• Fevers & night sweats• Recent infection, intravenous drug abuse, or immune compromise |

Back pain is common, and the majority of cases are due to benign skeletal (eg, osteoarthritis, spinal stenosis, disc herniation) or muscular (eg, muscle strain) conditions. The most common causes of back pain generally worsen with activity and improve with rest, postural modifications (eg, spinal stenosis worsens with back extension and is relieved with flexion), and analgesic therapy.

However, this patient's **constant** back pain that fails to improve with positional changes, rest, or analgesics is concerning for a more serious condition (infection, malignancy). This pattern of pain in an **older patient** (age >50) without a recent history of intravenous drug use should raise suspicion for a **neoplastic process**, particularly if the pain is worse at night (**nocturnal pain**). Other features that raise concern for malignancy include a personal history of cancer, weight loss, neurologic deficits (eg, weakness), and point





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

malignancy include a personal history of cancer, weight loss, neurologic deficits (eg, weakness), and point tenderness on the spinous processes.

Malignancies with a propensity for bony metastasis include **Prostate, Breast, Kidney, Thyroid, and Lung** (mnemonic: **Pb KTL**, or "**lead kettle**"). Prostate cancer is the most common malignancy in older men and frequently metastasizes to the axial skeleton and femur.

(Choice A) Degenerative disorders in the spine (eg, facet osteoarthritis) are typically relieved with rest and while in bed overnight; this patient's constant pain that persists overnight is more worrisome for malignancy.

(Choice B) Vertebral osteomyelitis (pain at rest, focal tenderness) and epidural abscess (nerve root compression, radicular symptoms) can be associated with intravenous drug use but typically occur following recent use, not decades later, and are usually associated with systemic symptoms (eg, fever, night sweats).

(Choice C) Inflammatory back pain (eg, spondyloarthropathy) is characterized by slowly progressive pain that is often worse at night. However, it is associated with prolonged morning stiffness (eg, hours) and improves with exercise. In addition, onset almost always occurs at age <45.

(Choice E) Back pain may be psychogenic (eg, factitious, malingering). Evidence of secondary gain (eg, litigation/compensation) and an unusual pattern of signs and symptoms can help identify these patients.



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

compression, radicular symptoms) can be associated with intravenous drug use but typically occur following recent use, not decades later, and are usually associated with systemic symptoms (eg, fever, night sweats).

(Choice C) Inflammatory back pain (eg, spondyloarthropathy) is characterized by slowly progressive pain that is often worse at night. However, it is associated with prolonged morning stiffness (eg, hours) and improves with exercise. In addition, onset almost always occurs at age <45.

(Choice E) Back pain may be psychogenic (eg, factitious, malingering). Evidence of secondary gain (eg, litigation/compensation) and an unusual pattern of signs and symptoms can help identify these patients.

Educational objective:

Clinical features that suggest a malignant cause of back pain include persistent pain at night, no relief with rest, onset at age >50, and systemic symptoms. Common malignancies with a propensity for bony metastasis include prostate, breast, kidney, thyroid, and lung.

Pathology

Rheumatology/Orthopedics & Sports

Prostate cancer

Subject

System

Topic

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1



Feedback



Suspend



End Block



Previous



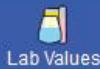
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Full Screen



Tutorial



Lab Values



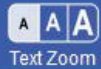
Notes



Calculator



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Text Zoom



Settings

A 45-year-old woman comes to the office for follow-up of arthritis. For the last year, she has had fatigue, weight loss, and progressive joint pain in the hands associated with prolonged morning stiffness. Past medical history includes hypothyroidism, for which she takes levothyroxine. The patient does not use tobacco or alcohol. Examination shows doughy swelling involving multiple metacarpophalangeal joints in both hands. Following initial diagnostic testing, a multidrug treatment regimen is started. Soon after treatment begins, she develops painful mouth ulcers and nausea. Liver function tests show new aspartate transaminase and alanine transaminase elevations. Which of the following medications is most likely responsible for the adverse effects seen in this patient?

- ☐ A. Hydroxychloroquine
- ☐ B. Methotrexate
- ☐ C. Minocycline
- ☐ D. Naproxen
- ☐ E. Prednisone



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

weight loss, and progressive joint pain in the hands associated with prolonged morning stiffness. Past medical history includes hypothyroidism, for which she takes levothyroxine. The patient does not use tobacco or alcohol. Examination shows doughy swelling involving multiple metacarpophalangeal joints in both hands. Following initial diagnostic testing, a multidrug treatment regimen is started. Soon after treatment begins, she develops painful mouth ulcers and nausea. Liver function tests show new aspartate transaminase and alanine transaminase elevations. Which of the following medications is most likely responsible for the adverse effects seen in this patient?

- ☐ A. Hydroxychloroquine (11%)
- ☒ B. Methotrexate (72%)
- ☐ C. Minocycline (2%)
- ☐ D. Naproxen (6%)
- ☐ E. Prednisone (7%)

Correct

72%
Answered correctly48 secs
Time Spent12/29/2020
Last Updated

Block Time Remaining: 00:34:06

TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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- ☒ B. Methotrexate (72%)
- ☐ C. Minocycline (2%)
- ☐ D. Naproxen (6%)
- ☐ E. Prednisone (7%)

Correct

72%



48 secs



12/29/2020

Block Time Remaining: 00:34:06

TUTOR

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient, a middle-aged woman with polyarthritis, morning stiffness, and systemic symptoms, has typical features of **rheumatoid arthritis (RA)**. **Methotrexate** is the preferred first-line disease-modifying treatment for most patients with moderate to severe RA. Methotrexate is a folate antimetabolite that halts purine and pyrimidine synthesis through competitive inhibition of **dihydrofolate reductase**.

Methotrexate preferentially inhibits growth of rapidly dividing cells, such as inflammatory and neoplastic cells. However, this inhibitory effect also causes toxicity to tissues with rapid cellular turnover, such as oral and gastrointestinal mucosa (**ulcerations**), hair follicles (alopecia), and bone marrow (pancytopenia). Methotrexate can also cause **hepatotoxicity** (hepatitis, fibrosis, cirrhosis) and pulmonary fibrosis.

(Choice A) Hydroxychloroquine is a well-tolerated antirheumatic drug used in mild RA and systemic lupus erythematosus. Its most significant toxicity is irreversible retinopathy, and patients should have regular ophthalmologic examinations.

(Choice C) Minocycline is a tetracycline antibiotic with weak antirheumatic activity. Common side effects include photosensitivity dermatitis.

(Choice D) Nonsteroidal anti-inflammatory drugs (NSAIDs [eg, naproxen]) are used for initial symptom relief in RA, although they do not prevent the long-term joint damage caused by the disease. Significant side effects include gastritis/gastric ulcers and acute kidney injury.



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Feedback



Suspend



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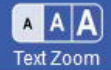
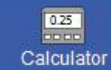
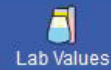
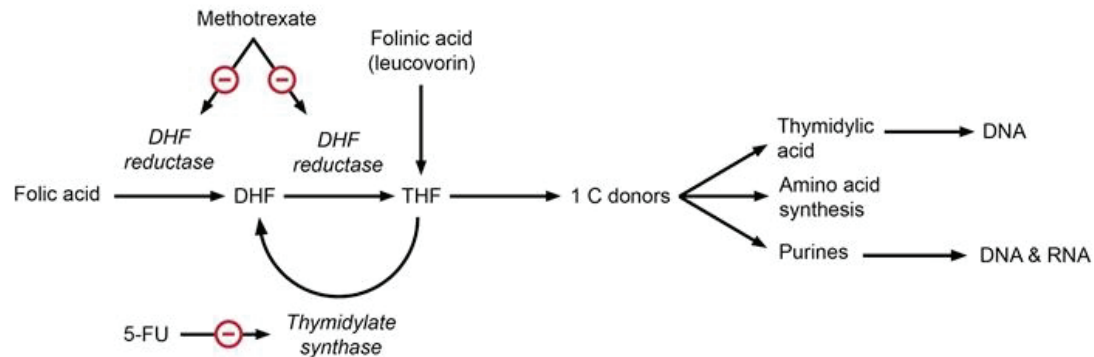


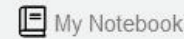
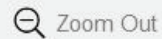
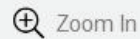
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Folic acid pathway



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5-FU = 5-fluorouracil; C = carbon; DHF = dihydrofolate; THF = tetrahydrofolate





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

erythematosus. Its most significant toxicity is irreversible retinopathy, and patients should have regular ophthalmologic examinations.

(Choice C) Minocycline is a tetracycline antibiotic with weak antirheumatic activity. Common side effects include photosensitivity dermatitis.

(Choice D) Nonsteroidal anti-inflammatory drugs (NSAIDs [eg, naproxen]) are used for initial symptom relief in RA, although they do not prevent the long-term joint damage caused by the disease. Significant side effects include gastritis/gastric ulcers and acute kidney injury.

(Choice E) Glucocorticoids are used for initial treatment and acute flares of RA. Short-term side effects include insomnia and hyperglycemia. Long-term side effects are significant and include weight gain, osteoporosis, and muscle weakness; these drugs also potentiate the risk of gastric ulcers in patients taking NSAIDs.

Educational objective:

Methotrexate is the preferred disease-modifying treatment for patients with moderate to severe rheumatoid arthritis. Significant adverse effects include stomatitis, bone marrow suppression, and liver function abnormalities.

References



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Feedback



Suspend



End Block



Previous



Next



Full Screen



Tutorial



Lab Values



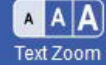
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 19-year-old woman is evaluated in the clinic due to right hand clumsiness. The patient injured the right upper extremity after falling off her bicycle 6 months ago. She has since had a "pins and needles" sensation in the right hand associated with mild weakness. The patient is worried as these symptoms are interfering with her piano lessons and she has an upcoming recital in 3 weeks. Physical examination shows decreased sensation over the fifth digit and a flattened hypothenar eminence. Triceps reflexes are 2+ and symmetric bilaterally. The nerve affected in this patient is commonly injured at which of the following locations?

- ☐ A. Carpal tunnel
- ☐ B. Coracobrachialis muscle
- ☐ C. Head of the radius
- ☐ D. Hook of the hamate
- ☐ E. Midshaft of the humerus
- ☐ F. Surgical neck of the humerus



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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- ☐ A. Carpal tunnel (4%)
- ☐ B. Coracobrachialis muscle (2%)
- ☐ C. Head of the radius (6%)
- ☒ D. Hook of the hamate (78%)
- ☐ E. Midshaft of the humerus (4%)
- ☐ F. Surgical neck of the humerus (2%)

Correct

78%



01 min, 10 secs



01/05/2021

Block Time Remaining: 00:35:16

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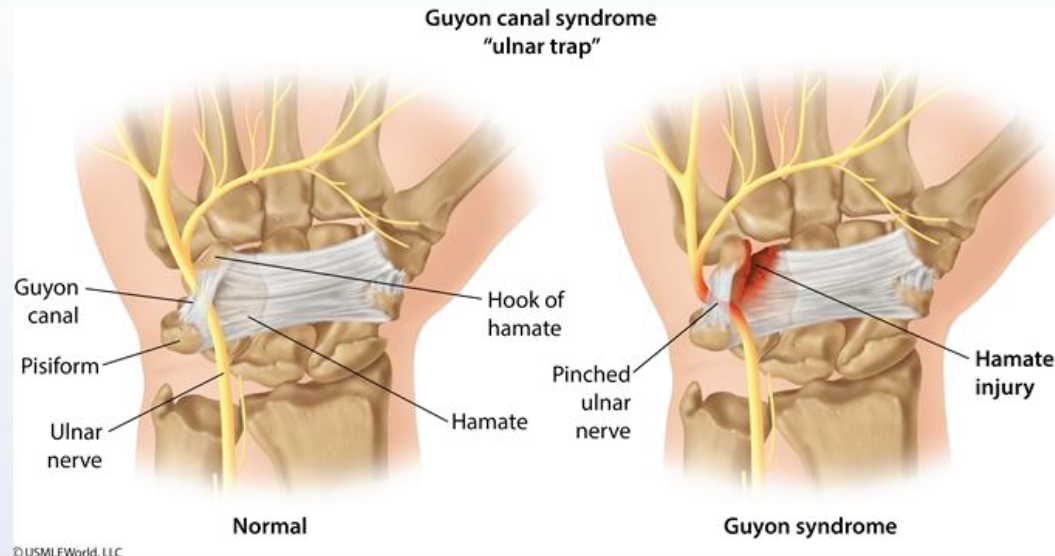
Feedback



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End Block



This patient's presentation is consistent with ulnar neuropathy. The **ulnar nerve** is a branch of the medial cord of the brachial plexus derived from the C8-T1 ventral rami. It enters the forearm after passing behind the medial epicondyle of the humerus. Within the forearm, it innervates the flexor carpi ulnaris and the medial portion of the flexor digitorum profundus. The nerve then enters the wrist between the **hook of the hamate** and the pisiform bone in a fibroosseous tunnel known as **Guyon's canal**. Here, it divides into a



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

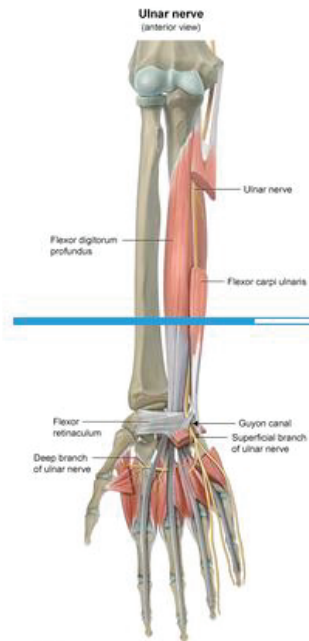


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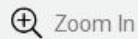


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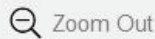
Exhibit Display

Nerves of the upper limb Important nerves in the arm

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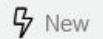
Zoom In



Zoom Out



Reset



New



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My Notebook



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Feedback



Suspend



End Block

Exhibit Display

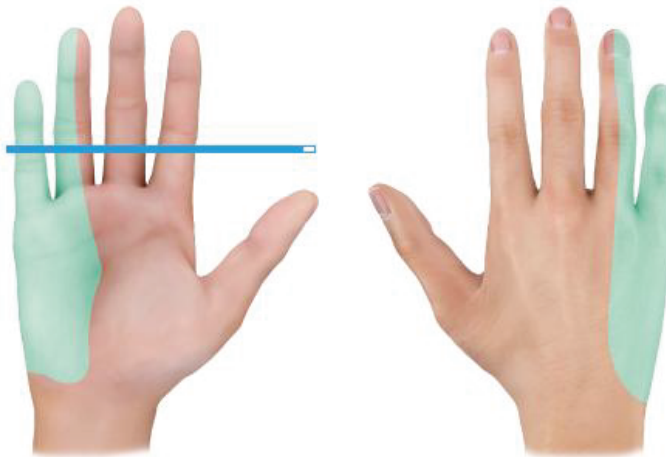
Nerves of the upper limb [Important nerves in the arm](#)

Ulnar nerve

Motor function

- Finger adduction
- Finger abduction other than the thumb
- Flexion of digits 4 & 5
- Wrist flexion & adduction

Cutaneous innervation



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

the medial epicondyle of the humerus. Within the forearm, it innervates the flexor carpi ulnaris and the

medial portion of the flexor digitorum profundus. The nerve then enters the wrist between the **hook of the hamate** and the pisiform bone in a fibroosseous tunnel known as **Guyon's canal**. Here, it divides into a superficial branch that provides sensation over the **medial 1½ digits** and hypothenar eminence and a deep motor branch that supplies most of the intrinsic muscles of the hand.

The ulnar nerve is most commonly injured at the elbow ("funny bone") due to trauma or nerve compression, but it can also be injured at the wrist as it runs through Guyon's canal. Nerve damage may cause sensory loss in the ulnar distribution with weakness on wrist flexion/adduction, finger abduction/adduction, and flexion of the fourth/fifth digits. The **hypothenar eminence** can appear flattened due to denervated muscle **atrophy**. Weakness of the lumbricals in the fourth/fifth digits may also produce an "ulnar claw" deformity during finger extension.

(Choice A) Carpal tunnel syndrome can result from any condition that reduces the size of the carpal tunnel and compresses the median nerve (eg, pregnancy, hypothyroidism). Patients typically have pain/paresthesias affecting the first 3½ digits. Thenar atrophy with weakness on thumb abduction/opposition may also be seen.

(Choice B) The coracobrachialis muscle lies deep to the biceps brachii and is perforated and innervated by the musculocutaneous nerve. Nerve injury may result in decreased strength on forearm flexion and



1



Feedback



Suspend



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

by the musculocutaneous nerve. Nerve injury may result in decreased strength on forearm flexion and sensory loss over the lateral forearm.

(Choice C) Subluxation of the radial head can injure the deep branch of the radial nerve during its passage through the supinator canal, leading to weakness during finger and thumb extension ("finger drop").

(Choice E) Fracture of the midshaft of the humerus typically results in radial nerve injury leading to paralysis of the hand and finger extensor muscles ("wrist drop") with sensory loss over the posterior forearm and dorsolateral hand.

(Choice F) Fracture of the surgical neck of the humerus may cause axillary nerve injury leading to paralysis of the deltoid and teres minor muscles with sensory loss over the lateral upper arm.

Educational objective:

The ulnar nerve can be injured at the medial epicondyle of the humerus ("funny bone") or in Guyon's canal near the hook of the hamate and pisiform bone in the wrist. Patients often have sensory loss over the medial 1½ digits and hypothenar eminence, and weakness on wrist flexion/adduction, finger abduction/adduction, and flexion of the fourth/fifth digits. The hypothenar eminence may flatten due to muscle atrophy.



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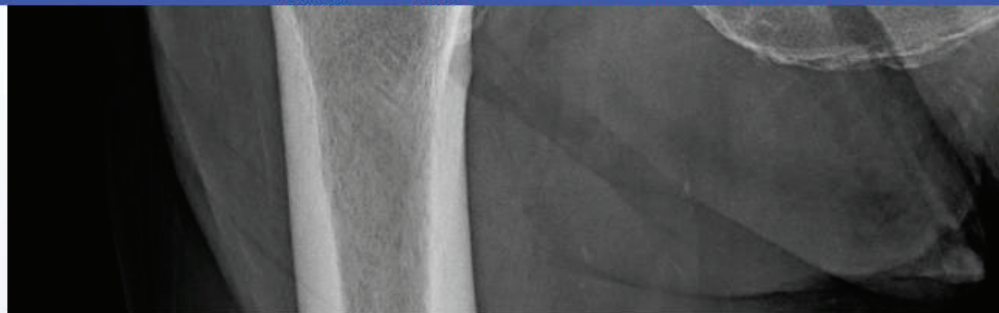
End Block

A 73-year-old woman is brought to the emergency department due to right hip pain. The patient was getting out of the shower when she slipped and fell directly on her right hip. She now has pain and swelling over the lateral aspect of her hip and cannot walk without assistance. Vital signs are within normal limits. Bilateral pedal pulses are normal, and sensation is intact. X-ray of the right hip is shown below.



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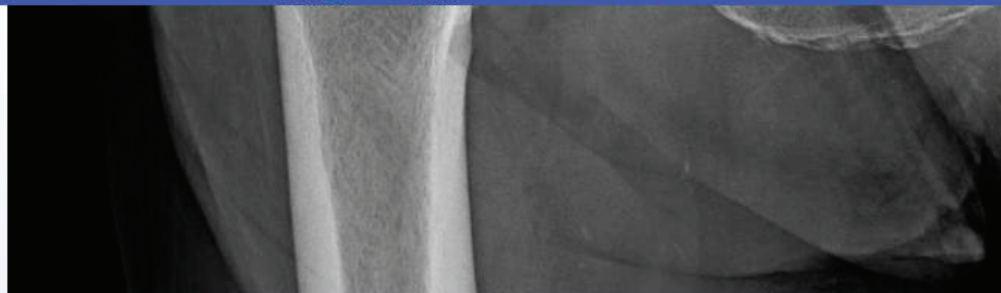
 Zoom In Zoom Out Reset New | Existing My Notebook



Examination of this patient will most likely show impaired function of which of the following muscles?

- ☐ A. Adductor magnus
- ☐ B. Gluteus medius
- ☐ C. Iliopsoas
- ☐ D. Rectus femoris
- ☐ E. Sartorius

Submit



Examination of this patient will most likely show impaired function of which of the following muscles?

- ☐ A. Adductor magnus (8%)
- ☒ B. Gluteus medius (44%)
- ☐ C. Iliopsoas (21%)
- ☐ D. Rectus femoris (9%)
- ☐ E. Sartorius (16%)

Correct

44%

25 secs

02/19/2021

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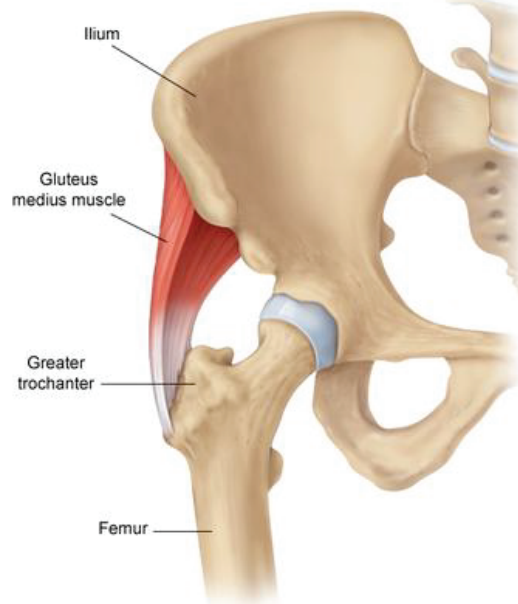
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Gluteus medius



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The pelvic bones and femoral trochanters provide sites of attachment for the large postural and ambulatory muscles of the hip girdle. Fractures involving these attachment sites are commonly caused by **high-velocity trauma** (eg, motor vehicle collisions, falls from height), but may occur even with ground-level falls (eg, getting out of the shower) in patients with **skeletal fragility** (eg, postmenopausal osteoporosis).

This patient's x-ray shows **avulsion** of the tip of the **greater trochanter of the femur**. The greater trochanter serves as the site of insertion for the **gluteus medius** muscle, which originates from the ilium. The main actions of the gluteus medius are **hip abduction** and stabilization of the pelvis during ambulation. Damage to the point of insertion on the greater trochanter can result in lateral hip pain with gait instability (ie, positive **Trendelenburg sign**) and weakness of abduction.

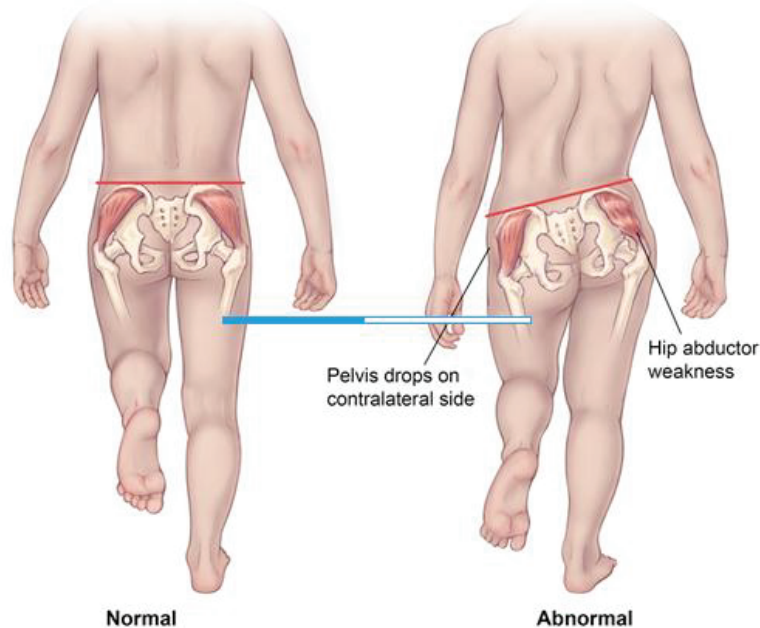
(Choice A) The ischiocondylar portion of the adductor magnus originates from the ischial tuberosity and inserts onto the medial condyle of the distal femur. Major functions include hip adduction and extension.

(Choice C) The **iliopsoas** is the union of iliacus and psoas major and inserts onto the lesser trochanter of the femur. It is the primary flexor of the hip.

(Choice D) The **rectus femoris** originates from the anterior inferior iliac spine, joins the other portions of the quadriceps femoris (ie, vastus lateralis, vastus medialis, and vastus intermedius) in a common quadriceps tendon, and attaches to the lower leg via the patella and patellar tendon. Because of its origin

Exhibit Display

Trendelenburg sign

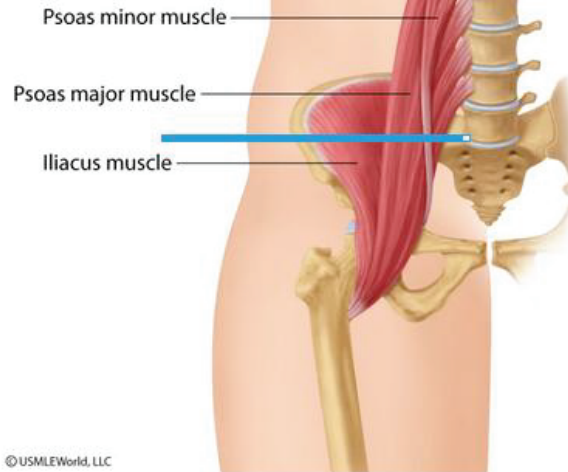


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Exhibit Display

The iliopsoas muscle



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Muscles of the hip

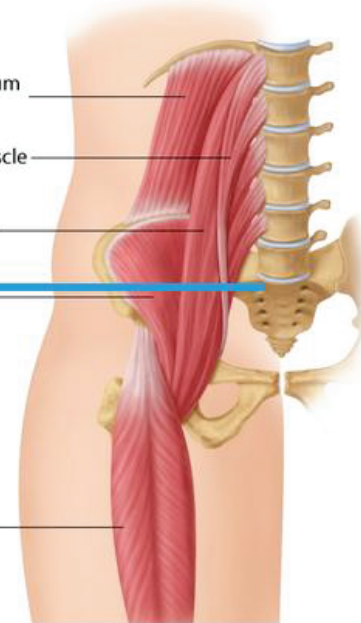
Quadratus lumborum
muscle

Psoas minor muscle

Psoas major muscle

Iliacus muscle

Rectus femoris
muscle



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(Choice D) The **rectus femoris** originates from the anterior inferior iliac spine, joins the other portions of the quadriceps femoris (ie, vastus lateralis, vastus medialis, and vastus intermedius) in a common quadriceps tendon, and attaches to the lower leg via the patella and patellar tendon. Because of its origin on the ilium, the rectus femoris contributes to hip flexion in addition to knee extension.

(Choice E) The **sartorius** originates from the anterior superior iliac spine and crosses the anterior thigh to insert with the pes anserinus (common tendon for the sartorius, gracilis, and semitendinosus muscles) onto the superomedial surface of the tibia. It aids in hip flexion, abduction, and external rotation.

Educational objective:

The greater trochanter of the femur serves as the site of insertion for the gluteus medius muscle, which is responsible for hip abduction and stabilization of the pelvis during ambulation. Fractures of the greater trochanter (eg, fragility fracture from a fall) can disrupt the integrity of the gluteus medius tendon and result in lateral hip pain with gait instability and weakness of hip abduction.

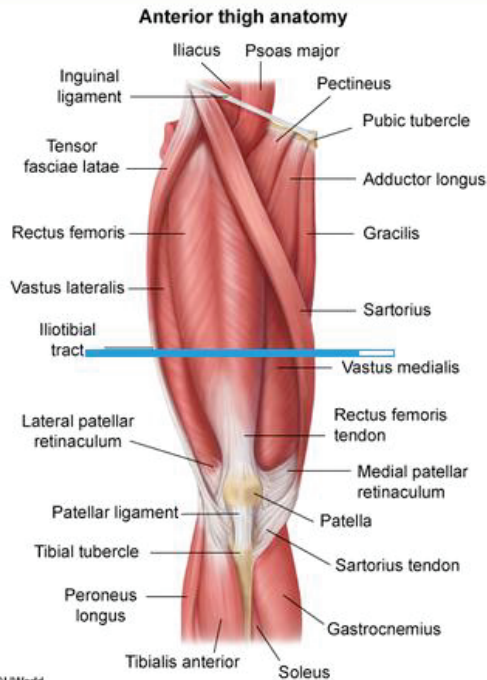
References

- Does isolated greater trochanter implication affect hip abductor strength and functions in intertrochanteric fracture?



(Choice D) The rectus femoris originates from the anterior inferior iliac spine, joins the other portions of

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Zoom Out

Reset

New | Existing

My Notebook



Previous



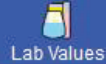
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Full Screen



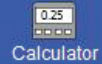
Tutorial



Lab Values



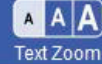
Notes



Calculator



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Text Zoom



Settings

A 35-year-old woman comes to the office with symmetric swelling and pain of her proximal interphalangeal, wrist, and knee joints. She reports that her 5-year-old son was seen by his pediatrician last week for a facial rash and fever. The patient's family history is significant for diabetes mellitus and gout in her father and rheumatoid arthritis in her mother. Her serum rheumatoid factor is negative. Conservative management with nonsteroidal anti-inflammatory drugs is recommended. The patient returns for follow-up 4 weeks later and reports that she discontinued the medication after 2 weeks due to gastrointestinal upset. However, her pain and swelling have decreased significantly. Which of the following is the most likely diagnosis?

- ☐ A. Gouty arthritis
- ☐ B. Herpes simplex virus infection
- ☐ C. Lyme disease
- ☐ D. Parvovirus infection
- ☐ E. Rheumatic fever
- ☐ F. Rheumatoid arthritis



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Feedback



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wrist, and knee joints. She reports that her 5-year-old son was seen by his pediatrician last week for a facial rash and fever. The patient's family history is significant for diabetes mellitus and gout in her father and rheumatoid arthritis in her mother. Her serum rheumatoid factor is negative. Conservative management with nonsteroidal anti-inflammatory drugs is recommended. The patient returns for follow-up 4 weeks later and reports that she discontinued the medication after 2 weeks due to gastrointestinal upset. However, her pain and swelling have decreased significantly. Which of the following is the most likely diagnosis?

- ☐ A. Gouty arthritis
- ☐ B. Herpes simplex virus infection
- ☐ C. Lyme disease
- ☐ D. Parvovirus infection
- ☐ E. Rheumatic fever
- ☐ F. Rheumatoid arthritis
- ☐ G. Systemic lupus erythematosus



and **mednatoio arthritis** in her mother. Her serum mednatoio factor is negative. Conservative management with nonsteroidal anti-inflammatory drugs is recommended. The patient returns for follow-up 4 weeks later and reports that she discontinued the medication after 2 weeks due to gastrointestinal upset. However, her pain and swelling have decreased significantly. Which of the following is the most likely diagnosis?

- ☐ A. Gouty arthritis (9%)
- ☐ B. Herpes simplex virus infection (0%)
- ☐ C. Lyme disease (2%)
- ☒ D. Parvovirus infection (57%)
- ☐ E. Rheumatic fever (6%)
- ☐ F. Rheumatoid arthritis (13%)
- ☐ G. Systemic lupus erythematosus (10%)

Correct

57%



01 min, 28 secs



10/24/2020

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Feedback



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| Parvovirus B19 | |
|-------------------|--|
| Pathology | <ul style="list-style-type: none">• Single-stranded DNA virus• Respiratory, congenital, or hematogenous transmission |
| Clinical features | <ul style="list-style-type: none">• Normal child: erythema infectiosum (fifth disease)• Normal adult: acute symmetric arthropathy• Chronic hemolytic anemia: Transient aplastic crisis |

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This patient and her child have typical features of **parvovirus B19** infection. Parvovirus is a small, single-stranded DNA virus with respiratory, congenital, or hematogenous transmission. Initial infection may cause a nonspecific viral syndrome with headache, coryza, and gastrointestinal symptoms. Parvovirus may subsequently cause 2 primary syndromes in immunocompetent patients:

- **Erythema infectiosum** (fifth disease), found primarily in children: This disease manifests as a bright red rash on the cheeks with circumoral pallor and fever. Patients may also have a generalized reticular rash on the arms, legs, and trunk.
- **Acute arthropathy**, found primarily in adults: This symmetric polyarthritits involves the proximal interphalangeal, metacarpal, knee, and ankle joints. The arthritis is self-limited and nondestructive.



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

reticular rash on the arms, legs, and trunk.

- **Acute arthropathy**, found primarily in adults: This symmetric polyarthritis involves the proximal interphalangeal, metacarpal, knee, and ankle joints. The arthritis is self-limited and nondestructive.

The initial nonspecific period of infection is associated with heavy viremia and viral shedding. By contrast, erythema infectiosum and acute arthropathy signify an active immune response with formation of **immune complexes** and minimal or undetectable viremia. These patients have much reduced infectivity.

(Choice A) Gout causes acute monoarthritis, usually affecting the lower extremity (great toe, ankle, knee).

(Choice B) Herpes simplex virus (HSV) infection causes oral or genital lesions characterized by grouped vesicles on an erythematous base. HSV does not usually cause arthritis.

(Choice C) Lyme disease causes a characteristic annular erythematous rash (erythema chronicum migrans). Asymmetric arthritis may develop in late or chronic Lyme disease.

(Choice E) In rheumatic fever, there may be migratory pain and swelling of the large joints in addition to fever, carditis, choreiform movements, and **erythema marginatum**. Rheumatic fever develops following streptococcal pharyngitis.

(Choice F) Rheumatoid arthritis may cause an acute polyarthropathy that is initially similar to parvovirus arthritis. The symptoms may be temporarily relieved with nonsteroidal anti-inflammatory drugs but would



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Feedback



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Mark

Previous

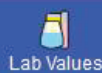
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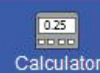
Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

reticular rash on the arms, legs, and trunk.

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:37:09

TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

migrans). Asymmetric arthritis may develop in late or chronic Lyme disease.

(Choice E) In rheumatic fever, there may be migratory pain and swelling of the large joints in addition to fever, carditis, choreiform movements, and [erythema marginatum](#). Rheumatic fever develops following streptococcal pharyngitis.

(Choice F) Rheumatoid arthritis may cause an acute polyarthropathy that is initially similar to parvovirus arthritis. The symptoms may be temporarily relieved with nonsteroidal anti-inflammatory drugs but would not resolve as promptly as they did in this patient. In addition, serum rheumatoid factor is usually, although not always, positive.

(Choice G) The typical initial onset of systemic lupus erythematosus is characterized by malaise, weight loss, malar facial rash, and arthralgias.

Educational objective:

Parvovirus B19 causes erythema infectiosum (fifth disease) in children and arthritis in adults. Parvovirus arthritis can mimic rheumatoid arthritis but is usually self-resolving.

References

- [Human parvovirus B19: a review.](#)



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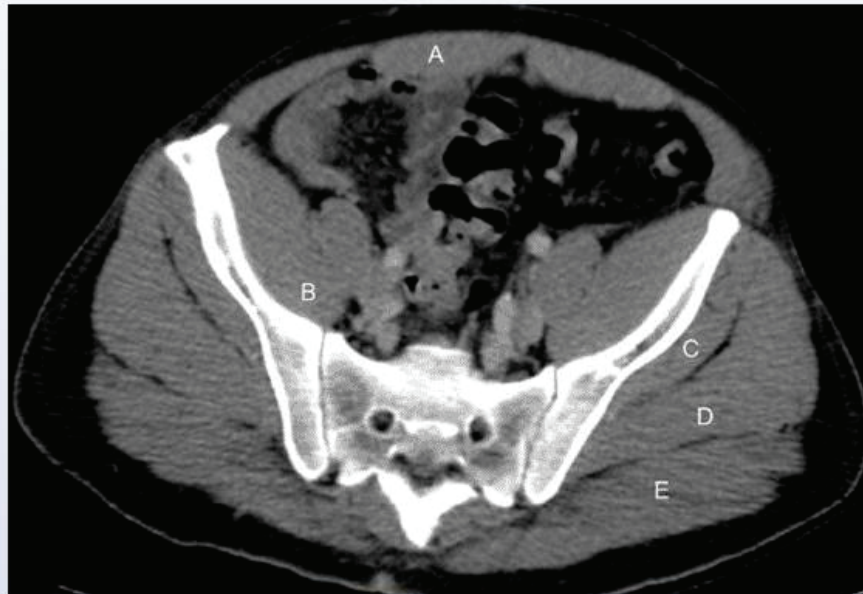


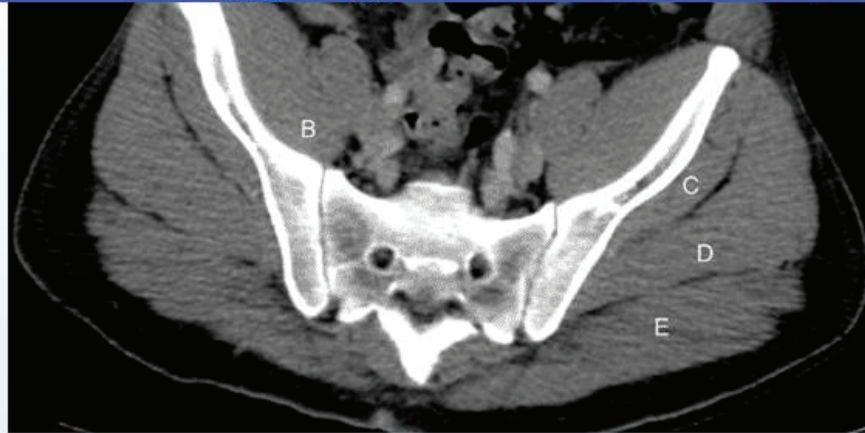
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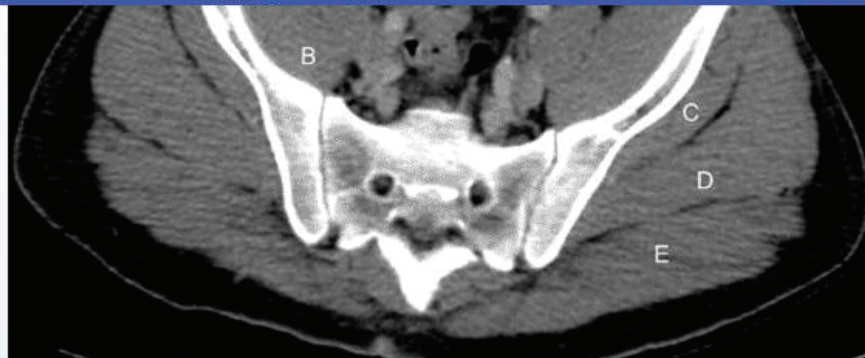
End Block

A 32-year-old male presents to the ER with sudden-onset heart palpitations. His blood pressure is 100/70 mmHg, and his heart rate is 160/min with regular rhythm. The physician instructs the patient to do the "Valsalva maneuver" to relieve these symptoms. Which of the following structures indicated on the pelvic CT image below is most important in performing the Valsalva maneuver?





- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E



- ✓ ☒ A.A (75%)
- ☐ B.B (15%)
- ☐ C.C (2%)
- ☐ D.D (2%)
- ☐ E.E (3%)

Correct

75%
Answered correctly

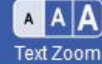
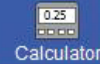
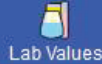
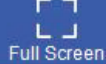
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The patient described in the question stem is experiencing paroxysmal supraventricular tachycardia. Treatment can be with vagal stimulation, such as carotid sinus massage or the Valsalva maneuver. Maneuvers that increase vagal tone increase the refractory period in the AV node and help prevent a reentrant circuit from conducting. If Valsalva measures fail, intravenous administration of adenosine is recommended.

The Valsalva maneuver is executed by forcibly exhaling against a closed glottis. This is done by taking a full inhalation, closing the glottis (i.e. holding one's breath), and subsequently bearing down-without exhaling-as one would during a bowel movement. The rectus muscles are recruited in this process, and they **(Choice A)** play the largest role in the development of the resultant elevated intraabdominal and intrathoracic pressure during this maneuver.

(Choice B) This structure is the iliacus muscle, a flexor of the hip that lies over the iliac fossa.

(Choice C) This structure is the gluteus minimus muscle. This muscle is innervated by the superior gluteal nerve and has the subtle, but important function of preventing the contralateral (non-weight-bearing) side of the pelvis from dipping when that leg is elevated off of the ground, as when one walks.

(Choice D) This structure is the gluteus medius muscle. This muscle has the same innervation and function as the gluteus minimus.

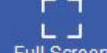




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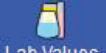
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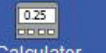
Tutorial



Lab Values



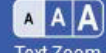
Notes



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Settings

(Choice B) This structure is the iliacus muscle, a flexor of the hip that lies over the iliac fossa.

(Choice C) This structure is the gluteus minimus muscle. This muscle is innervated by the superior gluteal nerve and has the subtle, but important function of preventing the contralateral (non-weight-bearing) side of the pelvis from dipping when that leg is elevated off of the ground, as when one walks.

(Choice D) This structure is the gluteus medius muscle. This muscle has the same innervation and function as the gluteus minimus.

(Choice E) This structure is the gluteus maximus muscle. This muscle is innervated by the inferior gluteal nerve and is the major extensor of the thigh at the hip.

Educational Objective:

The Valsalva maneuver increases vagal tone and can be used to abolish paroxysmal supraventricular tachycardia. The rectus abdominis is the most important muscle in achieving the increased intraabdominal and intrathoracic pressure of the Valsalva maneuver.

Anatomy

Rheumatology/Orthopedics & Sports

Abdominal wall muscles

Subject

System

Topic



Feedback



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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Settings

A 46-year-old gardener comes to the office due to knee pain. It began abruptly 3 days earlier and improved only minimally with acetaminophen. The patient spends hours on his knees several times a week while working. Past medical history is notable for hypertension and seasonal allergies. His current medications include lisinopril, loratadine, and fluticasone nasal spray. Examination of the lower extremity shows no visible erythema or abrasions, but there is sharp, localized pain on palpation. Passive range of motion is normal in all joints, but the patient has severe pain when walking around the room or climbing onto the examination table. Which of the following bursae is most likely affected in this patient?

- ☐ A. Anserine
- ☐ B. Gastrocnemius
- ☐ C. Prepatellar
- ☐ D. Semimembranosus (popliteal)
- ☐ E. Suprapatellar

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Block Time Remaining: 00:37:44

TUTOR

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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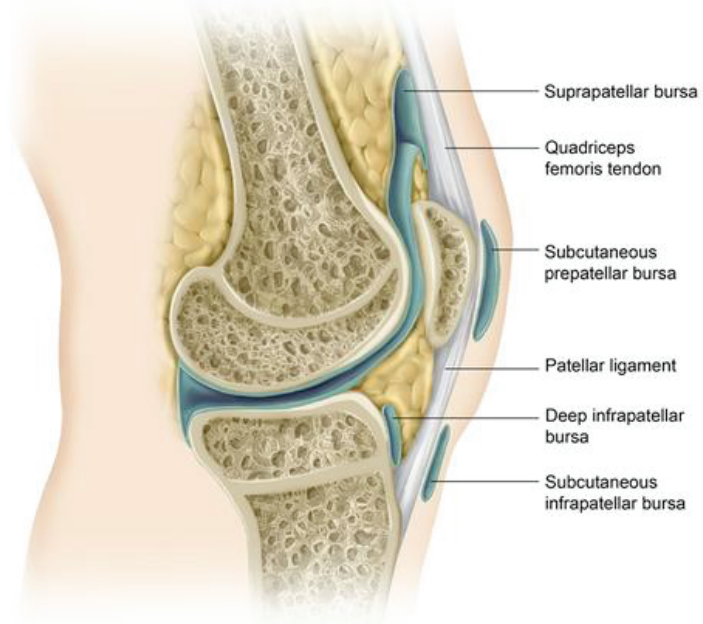
A 46-year-old **gardener** comes to the office due to knee pain. It began abruptly 3 days earlier and improved only minimally with acetaminophen. The patient spends hours **on his knees** several times a week while working. Past medical history is notable for hypertension and seasonal allergies. His current medications include lisinopril, loratadine, and fluticasone nasal spray. Examination of the lower extremity shows no visible erythema or abrasions, but there is sharp, localized pain on palpation. Passive range of motion is normal in all joints, but the patient has severe pain when walking around the room or climbing onto the examination table. Which of the following bursae is most likely affected in this patient?

- ☐ A. Anserine (3%)
- ☐ B. Gastrocnemius (2%)
- ☒ C. Prepatellar (65%)
- ☐ D. Semimembranosus (popliteal) (10%)
- ☐ E. Suprapatellar (17%)



Exhibit Display

Lateral knee



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A **bursa** is a fluid-filled synovial sac that serves to alleviate pressure and friction at bony prominences and ligamentous attachments throughout the body. Bursae are vulnerable to injury from acute trauma or chronic repetitive pressure and may also become inflamed due to infection (septic bursitis), crystalline arthropathy (eg, gout), or autoimmune conditions (eg, rheumatoid arthritis). Because bursae are located in prominent and exposed positions, the pain of bursitis may be exquisite, and point tenderness is typical. Other features of bursitis may include swelling and erythema, particularly with more superficial bursae. Active range of motion is often decreased or painful, but passive motion is usually normal as it results in less pressure on the inflamed bursa.

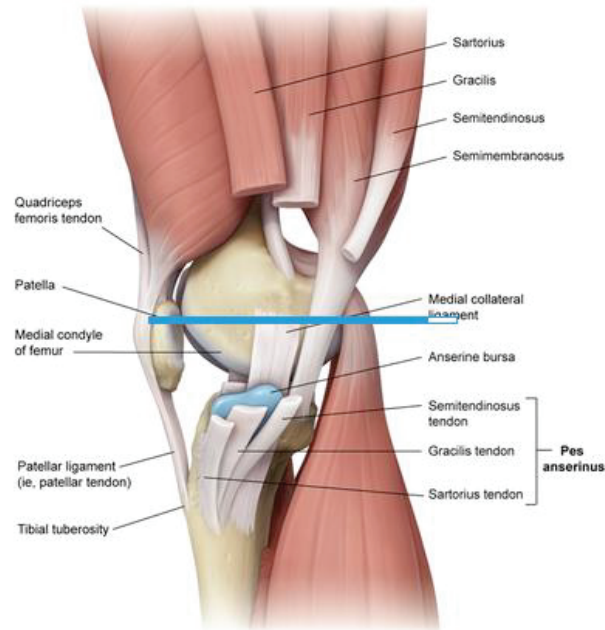
This patient with acute pain and localized tenderness associated with repetitive **anterior** knee trauma from kneeling has typical features of **prepatellar bursitis**, sometimes called "housemaid's knee." The prepatellar bursa is located between the patella and the overlying skin. Other occupations associated with prepatellar and infrapatellar bursitis include carpet layers, mechanics, and plumbers.

(Choice A) Anserine bursitis presents with pain along the medial knee and well-defined tenderness approximately 4 cm distal to the anteromedial joint margin of the knee. It frequently results from obesity or overuse in athletes.

(Choices B and D) Popliteal (Baker) cysts are caused by swelling of the gastrocnemius or

Exhibit Display

Medial knee & pes anserinus



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Zoom Out

Reset

New | Existing

My Notebook

(Choices B and D) Popliteal (Baker) cysts are caused by swelling of the gastrocnemius or

Block Time Remaining: 00:38:21

TUTOR

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

overuse in athletes.

(Choices B and D) Popliteal (Baker) cysts are caused by swelling of the gastrocnemius or semimembranosus bursa. They often form due to extrusion of synovial fluid from the knee joint into the bursa in patients with osteoarthritis or inflammatory joint disease.

(Choice E) The suprapatellar bursa is located anteriorly between the distal femur and quadriceps. Bursitis here is most often caused by a direct blow to the distal thigh or prolonged/repetitive quadriceps activity (eg, running).

Educational objective:

A bursa is a fluid-filled synovial sac that serves to alleviate pressure from bony prominences and reduce friction between muscles and tendons. Acute trauma or chronic repetitive pressure can cause injury, leading to localized pain and tenderness. Prepatellar bursitis causes anterior knee pain and is usually due to repetitive or prolonged kneeling.

Anatomy

Rheumatology/Orthopedics & Sports

Bursitis

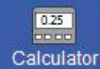
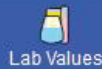
Subject

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Topic

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A 6-year-old girl is brought to the emergency department after falling from a chair onto her outstretched right arm. Physical examination shows swelling of the right elbow and tenderness to palpation over the distal humerus. Radial pulses are full and symmetric bilaterally. The patient is unable to cooperate with neurologic examination of the right hand due to significant pain. A peripheral intravenous line is placed, and analgesics are administered for pain control. X-rays show a supracondylar humeral fracture with anterolateral displacement of the proximal fracture fragment. Which of the following structures is most likely to be injured in this patient?

- ☐ A. Basilic vein
- ☐ B. Biceps tendon
- ☐ C. Median nerve
- ☐ D. Radial nerve
- ☐ E. Ulnar nerve

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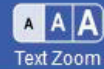
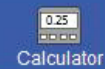
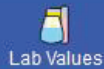
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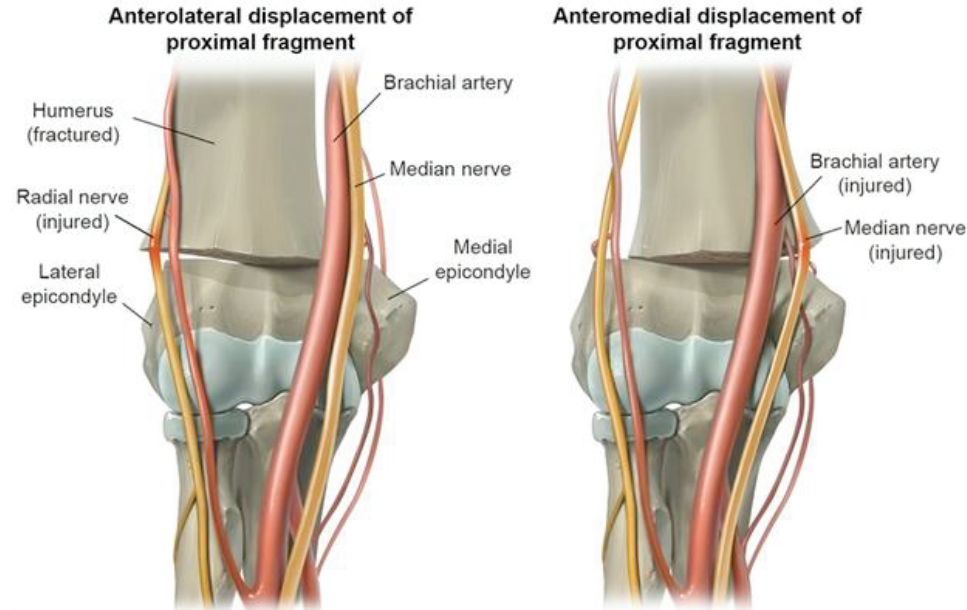
A 6-year-old girl is brought to the emergency department after falling from a chair onto her **outstretched** right arm. Physical examination shows swelling of the **right elbow** and tenderness to palpation over the **distal humerus**. Radial pulses are full and symmetric bilaterally. The patient is unable to cooperate with neurologic examination of the right hand due to significant pain. A peripheral intravenous line is placed, and analgesics are administered for pain control. X-rays show a **supracondylar humeral fracture** with **anterolateral displacement** of the proximal fracture fragment. Which of the following structures is most likely to be injured in this patient?

- ☐ A. Basilic vein (1%)
- ☐ B. Biceps tendon (4%)
- ☐ C. Median nerve (47%)
- ☒ D. Radial nerve (36%)
- ☐ E. Ulnar nerve (10%)



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Supracondylar humeral fracture



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hyperextension injuries (eg, falling onto an outstretched arm). These fractures carry a significant risk of

Supracondylar humeral fractures are common pediatric elbow fractures that characteristically occur after hyperextension injuries (eg, falling onto an outstretched arm). These fractures carry a significant risk of neurovascular compromise, especially if the fragments are displaced. The brachial artery, median nerve, and radial nerve all run anterior to the elbow, with the brachial artery and median nerve over the medial epicondyle and the **radial nerve** over the **lateral** epicondyle.

The median nerve and brachial artery are frequently injured in supracondylar fractures due to anteromedial displacement of the proximal fracture fragment (**Choice C**). However, this patient has **intact radial pulses** bilaterally (ie, sparing of the brachial artery) and **anterolateral displacement** of the proximal fracture fragment, making **radial nerve injury** more likely. Injury to the radial nerve at the elbow can result in wrist drop due to denervation of hand/finger extensor muscles, and sensory loss over the posterior forearm/dorsolateral hand.

(Choice A) The basilic vein runs superficially over the medial aspect of the elbow and is not commonly injured during supracondylar fractures.

(Choice B) The 2 heads of the biceps muscle originate from the scapula and insert onto the radius. Biceps tendon injury/rupture typically occurs in older patients following sudden extension of a flexed elbow



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice A) The basilic vein runs superficially over the medial aspect of the elbow and is not commonly injured during supracondylar fractures.

(Choice B) The 2 heads of the biceps muscle originate from the scapula and insert onto the radius. Biceps tendon injury/rupture typically occurs in older patients following sudden extension of a flexed elbow while contracting the biceps (eg, lifting a heavy object).

(Choice E) The ulnar nerve runs posterior to the medial epicondyle and can be injured with hyperflexion injuries (eg, falling onto a flexed elbow), resulting in posterior displacement of the proximal humerus or fracture of the medial epicondyle. Ulnar nerve injury at the elbow often presents with sensory loss over the fifth digit and half of the fourth digit, as well as weakness on flexion of the wrist and fourth/fifth digits.

Educational objective:

Supracondylar humeral fractures commonly occur after hyperextension of the elbow as a result of a fall onto an outstretched arm. The radial nerve runs along the anterolateral aspect of the elbow and is the structure most likely to be injured with anterolateral displacement of the proximal fracture fragment. The brachial artery runs with the median nerve on the anteromedial aspect of the elbow and will usually be spared in these patients (eg, intact radial pulse).

References



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 67-year-old man comes to the office with right tibial pain that started 3 months ago and has increased in intensity over time. He also has had progressive hearing impairment for the last year. Physical examination reveals local tenderness and a lumpy protuberance over the right tibia. After extensive evaluation, the patient undergoes a bone biopsy. The pathologist identifies numerous multinucleated cells, some containing over 100 nuclei. Which of the following factors is essential for the differentiation of the cells described by the pathologist?

- ☐ A. Fibroblast growth factor
- ☒ B. Insulin-like growth factors
- ☐ C. Osteoprotegerin
- ☐ D. Receptor activator of nuclear factor kappa-B ligand
- ☐ E. Transforming growth factor beta

Submit

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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- ☐ A. Fibroblast growth factor (13%)
- ☐ B. Insulin-like growth factors (4%)
- ☐ C. Osteoprotegerin (14%)
- ☒ D. Receptor activator of nuclear factor kappa-B ligand (52%)
- ☐ E. Transforming growth factor beta (13%)

Correct

 52%
Answered correctly 56 secs
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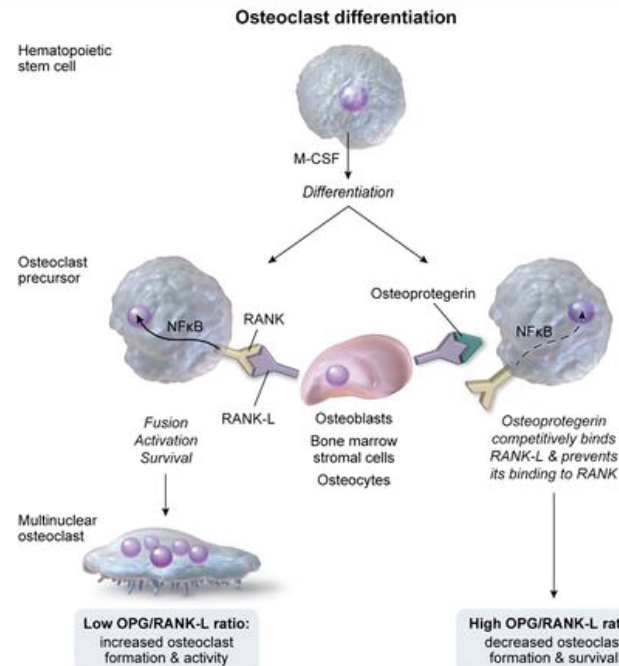


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Mark

Previous

Next



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increased osteoclast
formation & activitydecreased osteoclast
formation & survival

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This patient has pain and deformity of the long bones with hearing loss (due to bony deformity of the skull); these are typical features of **Paget's disease of bone**. The initial abnormality in Paget's disease is excessive osteoclastic bone resorption followed by increased bone formation by osteoblasts; this results in **high bone turnover** in the affected areas. The new bone formation is disorganized, and pagetic bone lesions typically appear on imaging as thickened areas of mixed sclerosis and lucency.

Osteoblasts are cells with a single nucleus that arise from mesenchymal stem cells found in the periosteum and bone marrow. In contrast, **osteoclasts** originate from the mononuclear phagocytic cell lineage and are ultimately formed when several precursor cells fuse to create a **multinucleated** mature cell. Osteoclasts in Paget's disease are typically very large and can have up to 100 nuclei (normal osteoclasts have 2-5). The 2 most important factors for osteoclastic differentiation, macrophage colony-stimulating factor (**M-CSF**) and receptor for activated nuclear factor kappa-B ligand (**RANK-L**), are produced by osteoblasts and bone marrow stromal cells.

Osteoprotegerin (OPG) is a physiologic decoy receptor that decreases binding of RANK-L to RANK.

Inhibition of RANK-L to RANK receptor interaction reduces the differentiation and survival of osteoclasts,



Feedback



Suspend



End Block



Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

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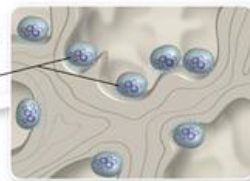
Paget disease of bone



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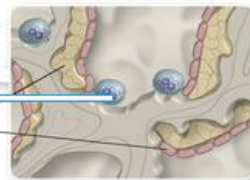
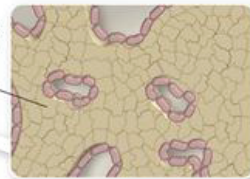
Osteolytic phase
(osteoclast dominant)

Osteoclasts

**Mixed phase**
(osteoclast + osteoblast)

New bone formation

Osteoblasts

**Osteosclerotic phase**
(osteoblast dominant)Weak, thickened,
woven bone

Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



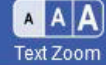
Notes



Calculator



Reverse Color



Text Zoom



Settings

Osteoprotegerin (OPG) is a physiologic decoy receptor that decreases binding of RANK-L to RANK. Inhibition of RANK-L to RANK receptor interaction reduces the differentiation and survival of osteoclasts, resulting in decreased bone resorption and increased bone density (**Choice C**). OPG loss-of-function mutations cause juvenile Paget's disease. A monoclonal antibody (denosumab) that inhibits the RANK/RANK-L interaction also leads to increased bone density and is commonly used for the treatment of osteoporosis.

(Choice A) Fibroblast growth factors (FGFs) regulate chondrogenesis and osteogenesis. FGFs induce proliferation of osteoblastic precursor cells and anabolic function of mature osteoblasts. Abnormalities in the FGF receptor result in the congenital short-limbed dwarfism known as achondroplasia.

(Choice B) Insulin-like growth factors (IGF-I and IGF-II) are synthesized by various tissues, including the liver and bone. IGF-I increases osteoblastic replication and collagen synthesis; it also decreases collagen degradation by inhibiting the enzyme matrix metalloproteinase-13 (MMP-13). The net effect of IGF-I on the bone is anabolic.

(Choice E) Transforming growth factor beta increases the replication of osteoblast precursors, leading to increased formation of mature osteoblasts. Transforming growth factor beta also increases collagen synthesis and decreases bone resorption by increasing osteoclastic apoptosis.



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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Educational objective:

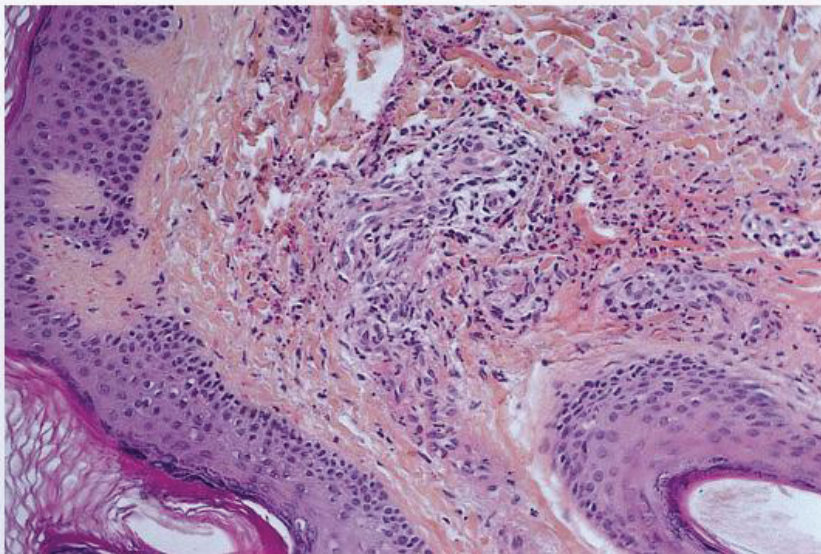
Osteoclasts originate from hematopoietic progenitor cells. Macrophage colony-stimulating factor and receptor for activated nuclear factor kappa-B ligand (RANK-L) play an important role in osteoclast differentiation. Paget's disease of bone is characterized by increased numbers of abnormal osteoclasts, excessive bone turnover and disorganized bone remodeling.

References

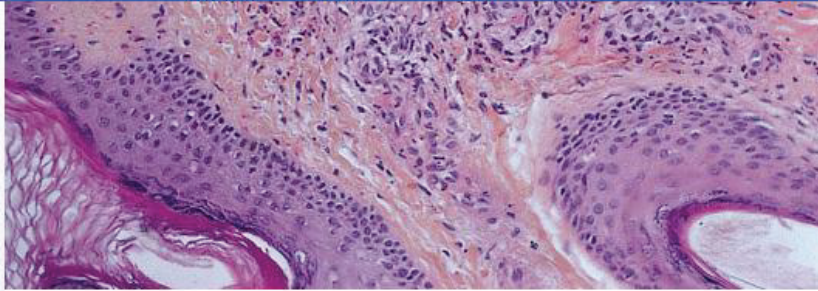
- [Regulation of NFATc1 in osteoclast differentiation.](#)



A 17-year-old boy comes to the office due to a skin rash that has been present for a day. One week ago, he had a sore throat that improved with oral penicillin therapy. Skin examination shows several violaceous, raised, nonblanchable lesions distributed over the bilateral lower extremities. Histologic findings of the biopsied rash are shown in the image below.



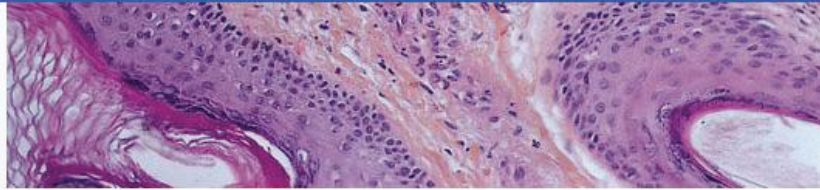
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Which of the following is the most likely diagnosis in this patient?

- ☐ A. Erythema nodosum
- ☐ B. Giant cell vasculitis
- ☐ C. Leukocytoclastic vasculitis
- ☐ D. Polyarteritis nodosa
- ☐ E. Rheumatoid nodules
- ☐ F. Urticaria



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Which of the following is the most likely diagnosis in this patient?

- ☐ A. Erythema nodosum (44%)
- ☐ B. Giant cell vasculitis (2%)
- ☒ C. Leukocytoclastic vasculitis (24%)
- ☐ D. Polyarteritis nodosa (6%)
- ☐ E. Rheumatoid nodules (7%)
- ☐ F. Urticaria (14%)

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24%

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Cutaneous small vessel vasculitis is a vasculitis that only affects the skin and typically arises due to drug or pathogen exposure (eg, hepatitis B or C virus). Drugs known to cause this condition include **penicillins**, cephalosporins, sulfonamides, phenytoin, and allopurinol. On skin examination, nonblanching **palpable purpura** is usually present and often involves the lower extremities. When biopsied, these skin lesions histologically demonstrate markedly inflamed small blood vessels with fibrinoid necrosis. In the first 24 hours, the perivascular inflammatory cell population consists primarily of **neutrophils** and fragmented neutrophilic nuclei (**leukocytoclastic vasculitis**), with mononuclear cells predominating in older lesions.

(Choice A) **Erythema nodosum** is a form of panniculitis (inflammation of subcutaneous fat) that typically presents with painful erythematous nodules in the lower extremities. Histopathologic findings include widening of connective tissue septae due to neutrophilic infiltration and fibrin exudation, followed by histiocyte and giant cell infiltration with septal fibrosis.

(Choice B) **Giant cell vasculitis** (temporal arteritis) affects medium- and large-sized arteries and typically presents with unilateral headache and jaw claudication in individuals age >50. Histopathologic findings include focal granulomatous inflammation of the media and internal elastic lamina fragmentation.

(Choice D) **Polyarteritis nodosa** is a transmural, necrotizing vasculitis that affects small- and medium-sized arteries. Patients typically present with systemic symptoms (eg, fatigue, fever, weight loss), renal failure,



Exhibit Display

Cutaneous small vessel vasculitis Leukocytoclastic vasculitis



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arteries. Patients typically present with systemic symptoms (red, fatigue, fever, weight loss, renal failure,

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Cutaneous small vessel vasculitis Leukocytoclastic vasculitis

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


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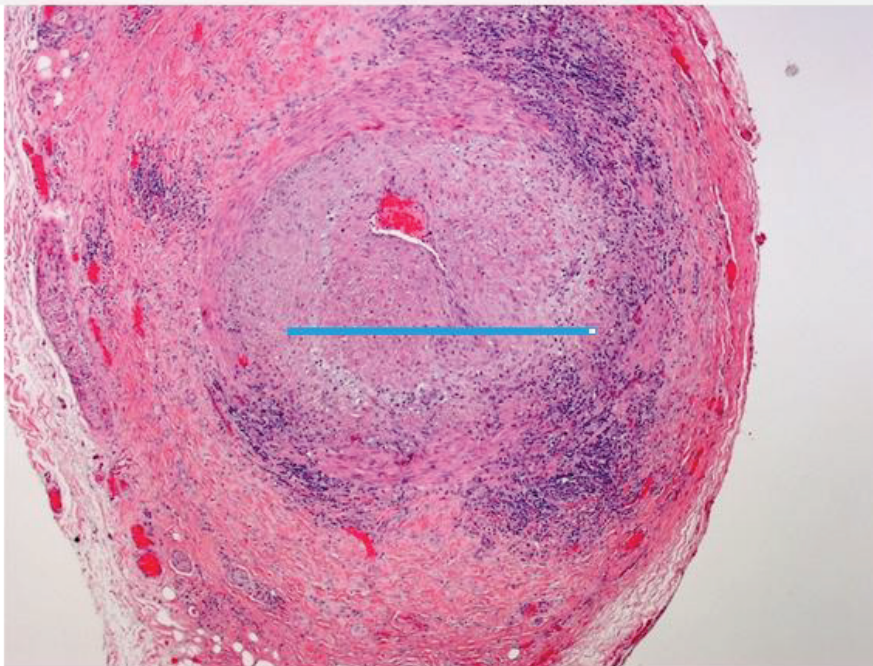


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Temporal arteritis Temporal arteritis

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arteries. Patients typically present with systemic symptoms (red, pain, fever, weight loss) renal failure.

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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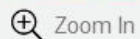
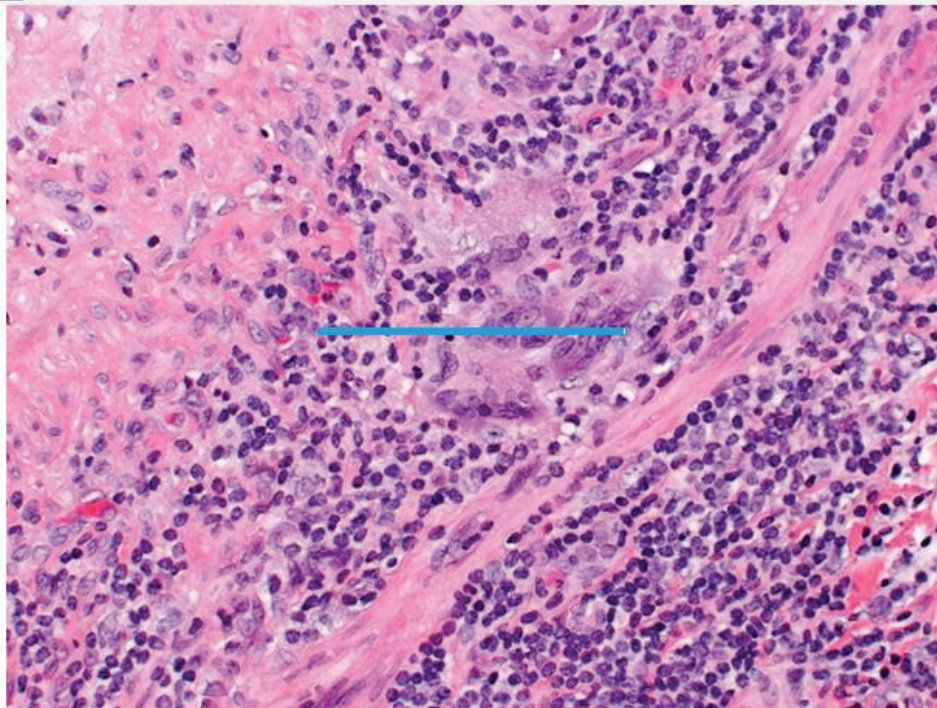


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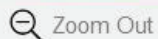


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Temporal arteritis Temporal arteritis

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My Notebook



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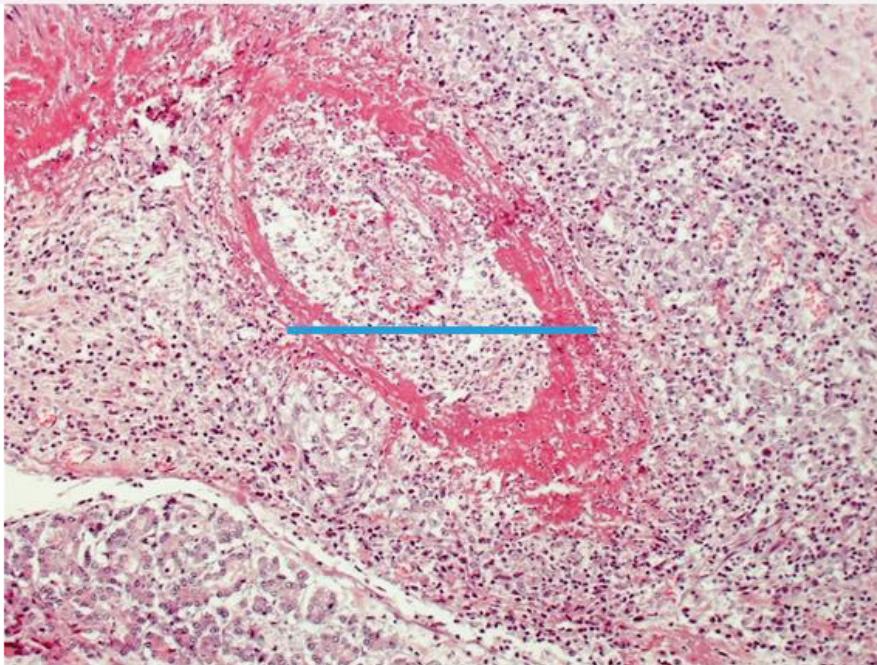
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Exhibit Display

Polyarteritis nodosa Polyarteritis nodosa



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

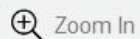
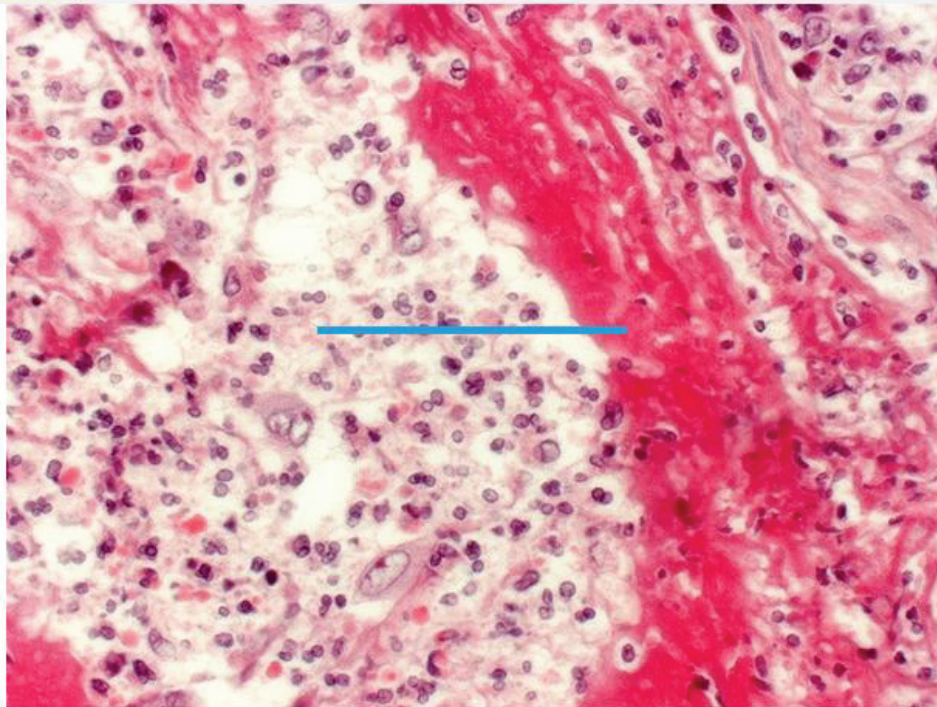


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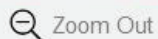


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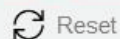
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Polyarteritis nodosa Polyarteritis nodosa

Zoom In



Zoom Out



Reset



New | Existing



My Notebook



0



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

include focal granulomatous inflammation of the media and internal elastic lamina fragmentation.

(Choice D) **Polyarteritis nodosa** is a transmural, necrotizing vasculitis that affects small- and medium-sized arteries. Patients typically present with systemic symptoms (eg, fatigue, fever, weight loss), renal failure, and abdominal pain/bloody stools due to ischemia of the involved organs.

(Choice E) **Subcutaneous rheumatoid nodules** appear as round, firm, nontender lesions that typically arise at pressure points (eg, olecranon process) in patients with advanced rheumatoid arthritis. Classic histopathologic findings include a necrotic center surrounded by palisading macrophages and lymphocytes.

(Choice F) **Urticaria** is often caused by medications; however, patients typically develop transient erythematous, raised, blanchable skin lesions. Histopathologic findings typically include superficial dermal edema with a mild perivascular infiltrate (rare neutrophils) and dilated lymphatic channels.

Educational objective:

Cutaneous small vessel vasculitis is associated with medication (eg, penicillins, cephalosporins) use and typically presents with palpable purpura in the lower extremities. Characteristic histopathologic findings include marked perivascular inflammation of small blood vessels with fibrinoid necrosis and a predominance of neutrophils and fragmented neutrophilic nuclei (leukocytoclastic vasculitis).

References



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include focal granulomatous inflammation of the media and internal elastic lamina fragmentation

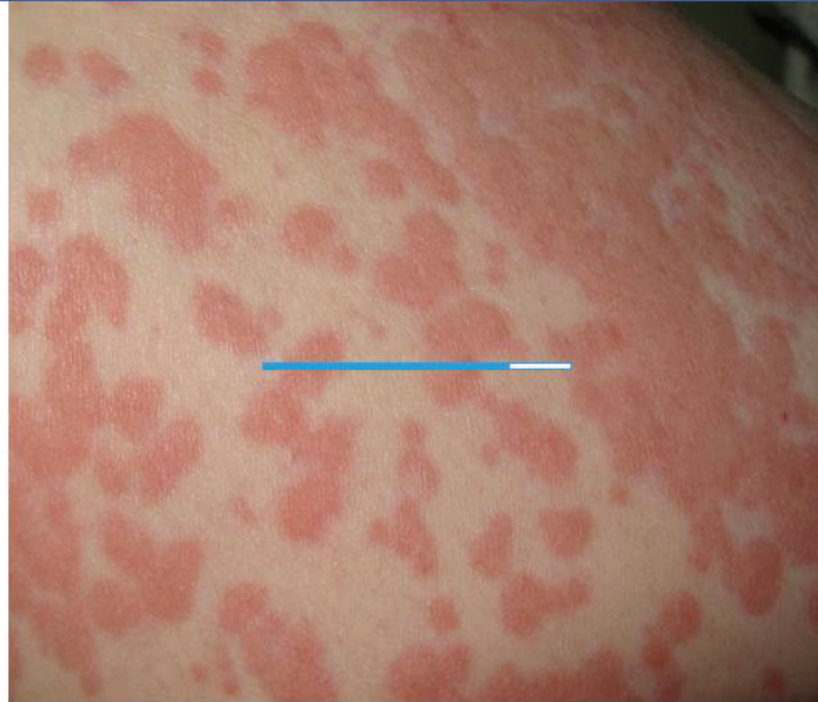
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References

include focal granulomatous inflammation of the media and internal elastic lamina fragmentation

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Zoom Out

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New | Existing

My Notebook

References

A 45-year-old male sustains a traumatic injury at work and presents to the emergency department with a deep laceration on the palm of his right hand. Three weeks later, actin-containing fibroblasts and increased metalloproteinase activity are detected at the site of injury. These findings are most likely related to which of the following complications?

- ☐ A. Wound dehiscence
- ☐ B. Ulceration
- ☒ C. Chronic infection
- ☐ D. Keloid formation
- ☐ E. Contracture

Submit

A 45-year-old male sustains a traumatic injury at work and presents to the emergency department with a deep laceration on the palm of his right hand. Three weeks later, actin-containing fibroblasts and increased metalloproteinase activity are detected at the site of injury. These findings are most likely related to which of the following complications?

- ☐ A. Wound dehiscence (14%)
- ☐ B. Ulceration (3%)
- ☐ C. Chronic infection (4%)
- ☒ D. Keloid formation (27%)
- ☐ E. Contracture (49%)

IncorrectCorrect answer
E 49%
Answered correctly 53 secs
Time Spent 01/30/2021
Last Updated



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Secreted by several different cell types (eg, fibroblasts, macrophages, neutrophils, synovial cells, some epithelial cells), matrix metalloproteinases (MMPs) primarily function in the degradation of collagen and other proteins in the extracellular matrix. MMP activity is important in wound healing, as it encourages both myofibroblast accumulation at the wound edges and scar tissue remodeling. The amassed myofibroblasts initiate wound contraction during healing by second intention. Contractures may occur when unusually pronounced MMP activity results in excessive wound contraction.

(Choice A) Wound dehiscence is the rupturing of a previously closed wound, and can result from insufficient granulation and scar tissue formation, inadequate wound contraction, or excessive mechanical stress. Such wound rupture most commonly occurs in abdominal wounds that are subject to increased intraabdominal pressure, which is not the case with this patient.

(Choice B) Ulceration of a wound typically results from inadequate vascularization during healing and is not associated with excessive matrix metalloproteinase or myofibroblast activity. Common sites of ulceration include lower extremity wounds in conjunction with atherosclerotic peripheral vascular disease.

(Choice C) Local infection is the most important cause of delayed wound healing. The delay results from persistent tissue injury and inflammation and is not known to be specifically related to excessive matrix metalloproteinase or myofibroblast activity.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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(Choice C) Local infection is the most important cause of delayed wound healing. The delay results from persistent tissue injury and inflammation and is not known to be specifically related to excessive matrix metalloproteinase or myofibroblast activity.

(Choice D) Keloids are hypertrophic scars in which excessive collagenous scar tissue deposited by fibroblasts permanently extends beyond the margins of the original wound. Keloids are not known to be specifically related to excessive matrix metalloproteinase or myofibroblast activity.

Educational Objective:

During wound healing, excessive matrix metalloproteinase activity and myofibroblast accumulation in the wound margins can result in contracture. Contractures produce deformities of the wound and surrounding tissues, most often on the palms, soles, anterior thorax, or at serious burn sites.

Pathology

Rheumatology/Orthopedics & Sports

Wound healing

Subject

System

Topic

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 54-year-old woman comes to the office due to right upper limb weakness and fatigue. She has no problem during most activities but develops symptoms when attempting to raise her arm overhead. The patient first noticed the symptoms after a recent hospitalization. On examination, there is no sensory loss in the upper extremities, but she has difficulty abducting her right arm past the horizontal position. The patient is instructed to press her outstretched arms against a wall, and the medial border of the right scapula lifts off the thoracic wall and becomes prominent. This patient was most likely hospitalized for which of the following conditions?

- ☐ A. Anterior dislocation of the shoulder joint
- ☐ B. Fracture of the middle third of the clavicle
- ☐ C. Mastectomy with axillary lymph node removal
- ☐ D. Total thyroidectomy
- ☐ E. Violent stretch between the head and the shoulder

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Feedback



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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Settings

A 54-year-old woman comes to the office due to right upper limb weakness and fatigue. She has no problem during most activities but develops symptoms when attempting to raise her arm overhead. The patient first noticed the symptoms after a recent hospitalization. On examination, there is no sensory loss in the upper extremities, but she has difficulty abducting her right arm past the horizontal position. The patient is instructed to press her outstretched arms against a wall, and the medial border of the right scapula lifts off the thoracic wall and becomes prominent. This patient was most likely hospitalized for which of the following conditions?

- ☐ A. Anterior dislocation of the shoulder joint (6%)
- ☐ B. Fracture of the middle third of the clavicle (4%)
- ☒ C. Mastectomy with axillary lymph node removal (79%)
- ☐ D. Total thyroidectomy (1%)
- ☒ E. Violent stretch between the head and the shoulder (7%)

Incorrect

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

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Settings

This patient has paralysis of the **serratus anterior** muscle due to **long thoracic nerve** injury. The serratus anterior originates on the surface of the first 8 ribs and inserts on the medial border of the scapula. It functions to stabilize and **rotate the scapula upward**. The deltoid and supraspinatus muscles abduct the arm up to the horizontal position, after which the serratus anterior and trapezius are required to rotate the glenoid cavity superiorly, thereby allowing complete abduction of the arm over the head.

Innervation of the serratus anterior is from the long thoracic nerve, which arises from the C5-C7 nerve roots via the **brachial plexus** and follows a lengthy course along the lateral chest wall. Injury to the nerve can occur during penetrating trauma or iatrogenically during **axillary lymph node dissection** or chest tube insertion. Paralysis of the serratus anterior causes **scapular winging** due to inability of the serratus to hold the scapula against the thorax. Patients will also show weakness in abducting the arm above horizontal due to impaired rotation of the scapula.

(Choice A) Anterior dislocation of the shoulder or fracture of the neck of the humerus can injure the axillary nerve. This causes paralysis of the deltoid and teres minor muscles and localized sensory loss in the upper arm.

(Choice B) Clavicular fracture only occasionally causes neurovascular compromise, usually involving the



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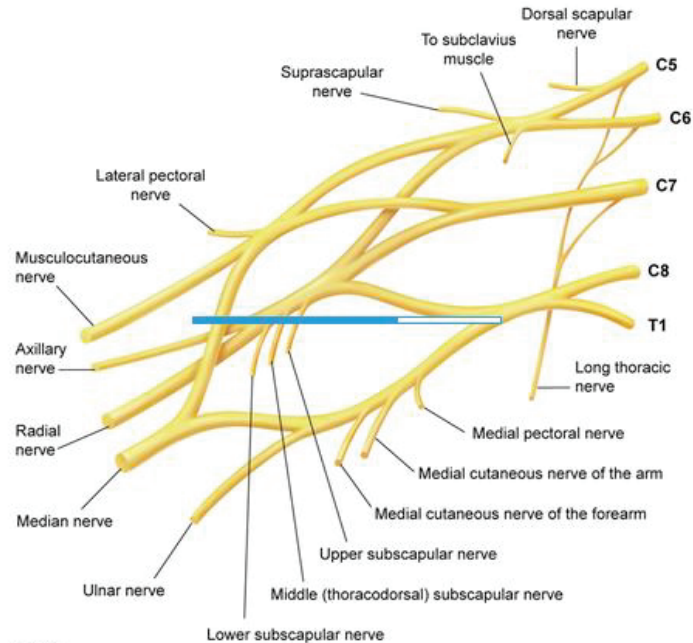
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Brachial plexus



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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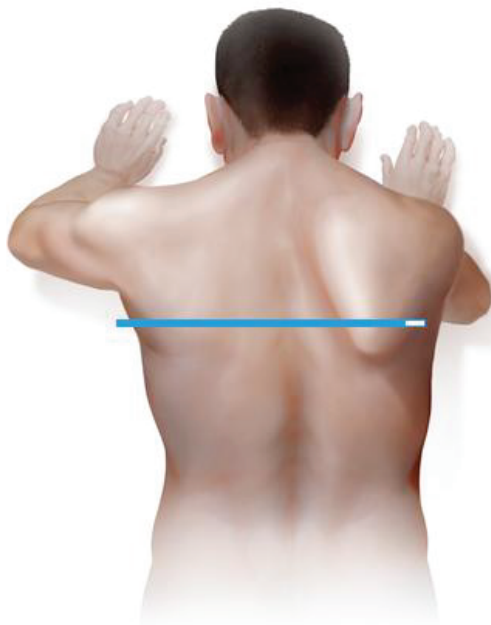
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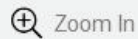
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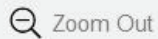
Winging of scapula



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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the upper arm.

(Choice B) Clavicular fracture only occasionally causes neurovascular compromise, usually involving the subclavian vessels and supraclavicular nerve.

(Choice D) Thyroidectomy may cause injury to the recurrent laryngeal nerve. Injury causes weakness of the posterior cricoarytenoid muscles, with hoarseness and impaired breathing.

(Choice E) Injury to the upper brachial plexus (musculocutaneous and suprascapular nerves) can occur due to traction between the head and shoulder. This can occur in the neonate due to dystocia or in the adult from violent injury. The resulting **palsy** is characterized by shoulder adduction, elbow extension, and forearm pronation.

Educational objective:

Dissection of the axillary lymph nodes can injure the long thoracic nerve. This results in weakness of the serratus anterior with winging of the scapula and impaired abduction of the shoulder past the horizontal.

References

- [Long thoracic nerve injury in breast cancer patients treated with axillary lymph node dissection.](#)

Anatomy Rheumatology/Orthopedics & Sports Brachial plexus

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Previous



Next



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Lab Values



Notes



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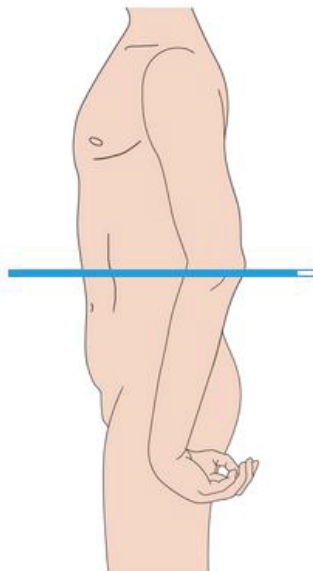


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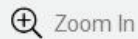
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Upper plexus lesions

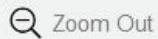
Bellman's or Waiter's tip pose



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A 38-year-old woman comes to the office due to abdominal pain. For the last 2-3 weeks, she has had increasingly severe abdominal pain associated with watery diarrhea. The patient has a history of Crohn disease treated for the last year with adalimumab, which has controlled the symptoms until now. Vital signs are normal except for a temperature of 37.8 C (100 F). Examination shows moderate tenderness in the right lower quadrant with no peritoneal signs. Laboratory results show an undetectable trough adalimumab level. Which of the following is the most likely explanation for this patient's worsening symptoms?

- ☐ A. Development of antidrug antibodies
- ☐ B. Formation of insoluble complexes at the injection site
- ☐ C. Increased enterohepatic drug recirculation
- ☐ D. Increased renal drug elimination
- ☐ E. Induction of cytochrome P-450 enzymes

Submit



A 38-year-old woman comes to the office due to abdominal pain. For the last 2-3 weeks, she has had increasingly severe abdominal pain associated with watery diarrhea. The patient has a history of Crohn disease treated for the last year with adalimumab, which has controlled the symptoms until now. Vital signs are normal except for a temperature of 37.8 C (100 F). Examination shows moderate tenderness in the right lower quadrant with no peritoneal signs. Laboratory results show an undetectable trough adalimumab level. Which of the following is the most likely explanation for this patient's worsening symptoms?

- ☒ A. Development of antidrug antibodies (55%)
- ☐ B. Formation of insoluble complexes at the injection site (13%)
- ☐ C. Increased enterohepatic drug recirculation (6%)
- ☐ D. Increased renal drug elimination (9%)
- ☒ E. Induction of cytochrome P-450 enzymes (14%)

Incorrect

Correct answer



55%

Answered correctly



01 min, 46 secs

Time Spent



01/28/2021

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This patient with Crohn disease initially responded to treatment with adalimumab but subsequently experienced treatment failure with a relapse of symptoms after nearly a year of therapy. **Adalimumab** is a recombinant human IgG that binds **tumor necrosis factor-alpha** (TNF-alpha), an inflammatory cytokine involved in promoting leukocyte migration, neutrophil and macrophage function, and granuloma integrity. Adalimumab prevents TNF-alpha from associating with its cell-surface receptors, blocking its pro-inflammatory effects. TNF-alpha inhibitors are used for a variety of inflammatory disorders such as Crohn disease, psoriasis, and rheumatoid arthritis.

However, use of adalimumab can induce the formation of **antidrug antibodies** (ADAs), which reduce the activity of the agent and lead to more rapid drug clearance and lower trough levels between doses. Patients with ADAs against adalimumab typically experience **declining effectiveness** of treatment and can develop hypersensitivity reactions after administration. The formation of ADAs can also be seen with other immunoglobulin-based anti-TNF agents (eg, infliximab) but is uncommon with etanercept, a recombinant TNF-receptor fusion protein.

(Choice B) Glargine is a long-acting insulin analogue that forms insoluble complexes. This leads to the formation of microprecipitates at the injection site that then slowly dissolve and are released into the circulation throughout the day. Adalimumab is given as a subcutaneous injection but does not form insoluble complexes at the injection site.





formation of microprecipitates at the injection site that then slowly dissolve and are released into the circulation throughout the day. Adalimumab is given as a subcutaneous injection but does not form insoluble complexes at the injection site.

(Choice C) Enterohepatic recirculation of certain cancer chemotherapeutic agents (eg, irinotecan) can lead to increased exposure of the intestinal mucosa to the agent and significant gastrointestinal toxicity. However, monoclonal antibodies do not undergo enterohepatic recirculation.

(Choice D) Adalimumab and other therapeutic monoclonal antibodies are eliminated primarily by degradation via receptor-mediated endocytosis in the reticuloendothelial system. Renal elimination of adalimumab can lead to increased drug clearance in patients with protein-losing glomerular disorders but otherwise does not significantly affect pharmacokinetics.

(Choice E) Cytochrome P-450 enzyme inducers (eg, rifampin, carbamazepine, phenobarbital) can cause accelerated clearance of drugs that are metabolized primarily in the liver. Adalimumab does not undergo metabolism by the P-450 system.

Educational objective:

Adalimumab is a recombinant human IgG that binds tumor necrosis factor-alpha (TNF-alpha). Antidrug antibodies can develop against adalimumab (or other immunoglobulin-based anti-TNF agents) that can



lead to increased exposure of the intestinal mucosa to the agent and significant gastrointestinal toxicity. However, monoclonal antibodies do not undergo enterohepatic recirculation.

(Choice D) Adalimumab and other therapeutic monoclonal antibodies are eliminated primarily by degradation via receptor-mediated endocytosis in the reticuloendothelial system. Renal elimination of adalimumab can lead to increased drug clearance in patients with protein-losing glomerular disorders but otherwise does not significantly affect pharmacokinetics.

(Choice E) Cytochrome P-450 enzyme inducers (eg, rifampin, carbamazepine, phenobarbital) can cause accelerated clearance of drugs that are metabolized primarily in the liver. Adalimumab does not undergo metabolism by the P-450 system.

Educational objective:

Adalimumab is a recombinant human IgG that binds tumor necrosis factor-alpha (TNF-alpha). Antidrug antibodies can develop against adalimumab (or other immunoglobulin-based anti-TNF agents) that can block its interaction with TNF-alpha, preventing the drug from functioning and leading to more rapid drug clearance.

References

- [The impact of anti-drug antibodies on drug concentrations and clinical outcomes in rheumatoid arthritis](#)

A 49-year-old man comes to the office due to "aching bones." He has a 2-month history of insidious-onset pain that is most pronounced in the back, pelvis, and lower extremities. The pain is dull and increases after weight-bearing activities. The patient has no prior medical conditions and takes no medications. He emigrated from Central Africa 5 years ago and works overnight shifts as a cab driver. Vital signs are within normal limits. Physical examination shows normal muscle strength in the upper and lower extremities bilaterally. A thorough laboratory evaluation establishes the diagnosis. After discussing the likely cause of his condition, the patient starts spending more time outdoors in the sun. Which of the following enzymatic steps will most likely be affected by this change in activity?

7-dehydrocholesterol



Cholecalciferol



25-hydroxyvitamin D3



24,25-dihydroxyvitamin D3





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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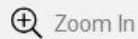
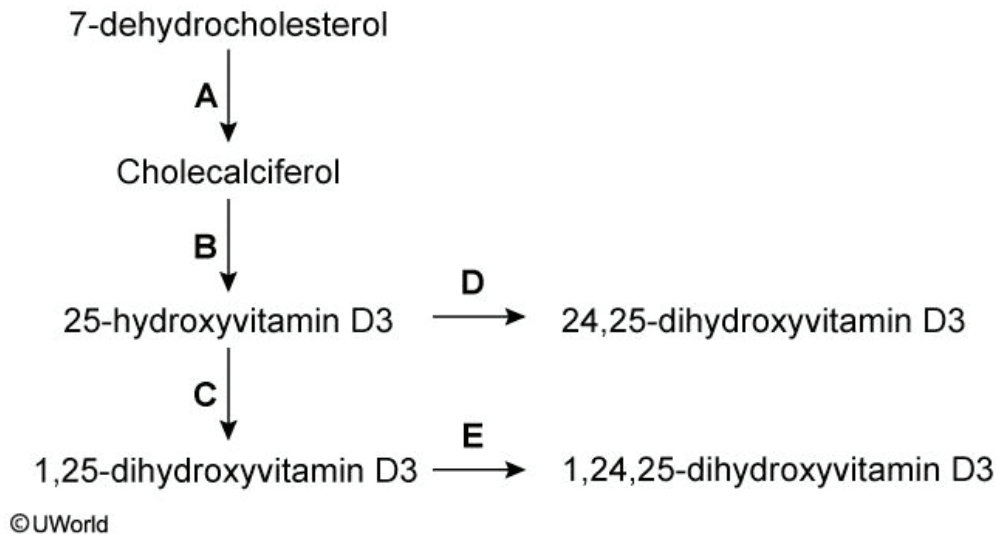


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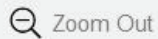


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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E

Submit

Cholecalciferol

B
↓

25-hydroxyvitamin D3

D
→

24,25-dihydroxyvitamin D3

C
↓

1,25-dihydroxyvitamin D3

E
→

1,24,25-dihydroxyvitamin D3

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☒ A.A (63%)☐ B.B (17%)☐ C.C (13%)☐ D.D (3%)☐ E.E (1%)

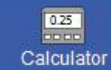
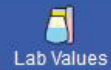
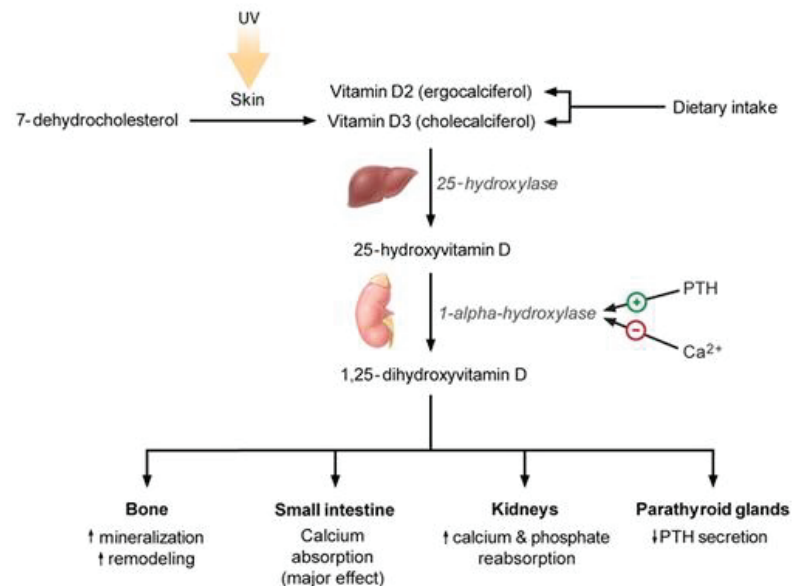
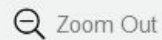
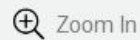


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Normal vitamin D metabolism



PTH = parathyroid hormone.
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Previous



Next



Full Screen



Tutorial



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Notes



Calculator



Reverse Color



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On exposure to **sunlight**, **7-dehydrocholesterol** (provitamin D3) in the skin absorbs ultraviolet (UV) B rays. This opens the B ring of 7-dehydrocholesterol, forming previtamin D3, which then undergoes thermal isomerization to form **vitamin D3** (cholecalciferol). Vitamin D3 is then hydroxylated in the liver to 25-hydroxyvitamin D and subsequently to 1,25-hydroxyvitamin D (the active form) in the kidneys.

Vitamin D deficiency can lead to osteomalacia with bone pain or tenderness, muscle weakness or cramps, gait abnormalities, and increased fracture risk. Factors associated with limited UV exposure and increased risk of vitamin D deficiency include the following:

- **Reduced time outdoors:** elderly individuals, patients living in residential care or who are frequently hospitalized, people who avoid going outdoors due to high risk of skin cancer
- **Low UV sun exposure:** individuals living at extreme northern or southern latitudes
- **Predominantly nocturnal lifestyle:** shift work or occupations requiring overnight work
- **Blockade of sunlight exposure:** people who use high-grade sunblock or wear full-coverage clothing
- **Reduced UV penetration:** individuals with heavily pigmented skin

(Choices B and C) The conversion of vitamin D2 and D3 to 25-hydroxycholecalciferol by 25-hydroxylase in the liver is primarily regulated by feedback inhibition from 25-hydroxycholecalciferol. The conversion to 1,25-dihydroxycholecalciferol by 1-alpha-hydroxylase in the kidney is primarily regulated by parathyroid



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choices B and C) The conversion of vitamin D2 and D3 to 25-hydroxycholecalciferol by 25-hydroxylase

in the liver is primarily regulated by feedback inhibition from 25-hydroxycholecalciferol. The conversion to 1,25-dihydroxycholecalciferol by 1-alpha-hydroxylase in the kidney is primarily regulated by parathyroid hormone (PTH) and plasma calcium levels. Neither of these steps takes place in the skin or is affected by sunlight exposure.

(Choices D and E) 25-hydroxyvitamin D-24-hydroxylase converts 25- and 1,25-dihydroxyvitamin D into inactive 24-hydroxylated metabolites. It is upregulated by 1,25-dihydroxyvitamin D (to prevent excess vitamin D activity) and suppressed by parathyroid hormone (to facilitate replenishment of circulating calcium levels) and thus functions as a counter-regulatory homeostatic enzyme. However, it is not affected by sunlight.

Educational objective:

Sunlight exposure catalyzes conversion of 7-dehydrocholesterol to cholecalciferol (vitamin D3) in the skin. Subsequent 25-hydroxylation in the liver and 1-hydroxylation in the kidneys produce 1,25-dihydroxyvitamin D, the active form. Inadequate exposure to sunlight can lead to vitamin D deficiency.

References

- [Sunlight, ultraviolet radiation, vitamin D and skin cancer: how much sunlight do we need?](#)



1



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Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



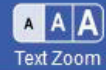
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Physiologists are studying the biomolecular mechanisms underlying skeletal muscle contraction. They have been analyzing muscle fibers obtained from knockout mice to determine how different cellular substances influence muscular contraction. Striated muscle fibers obtained from a specific mouse embryo fail to contract in response to a substance normally released from the sarcoplasmic reticulum. A deficiency of which of the following would best explain this finding?

- ☐ A. Acetylcholine
- ☐ B. Epinephrine
- ☐ C. Calmodulin
- ☐ D. Myosin light-chain kinase
- ☐ E. Troponin

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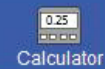
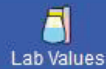
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Physiologists are studying the biomolecular mechanisms underlying skeletal muscle contraction. They have been analyzing muscle fibers obtained from knockout mice to determine how different cellular substances influence muscular contraction. Striated muscle fibers obtained from a specific mouse embryo fail to contract in response to a substance normally released from the sarcoplasmic reticulum. A deficiency of which of the following would best explain this finding?

- ☐ A. Acetylcholine (4%)
- ☐ B. Epinephrine (0%)
- ☐ C. Calmodulin (18%)
- ☐ D. Myosin light-chain kinase (9%)
- ☒ E. Troponin (67%)

Correct

67%
Answered correctly

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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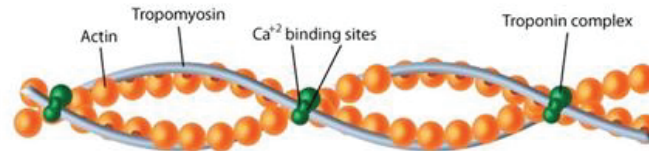
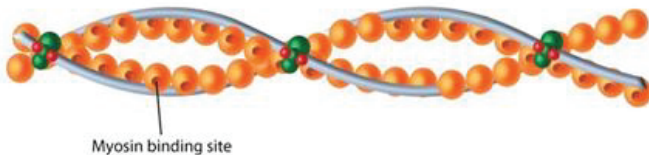


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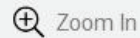
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 Ca^{+2} modulation of actin binding sites

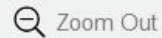
Myosin binding sites blocked

Troponin- Ca^{+2} complex
pulls tropomyosin away,
exposing myosin binding sites

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice A) Acetylcholine is the neurotransmitter that initiates muscle contraction in response to motor neuron stimulation. Acetylcholine release from the motor neuron opens post-synaptic ligand-gated ion channels, resulting in depolarization of the muscle cell. Depolarization then causes release of Ca^{2+} from the sarcoplasmic reticulum.

(Choice B) Epinephrine is a catecholamine that is not directly involved in skeletal muscle contraction. However, epinephrine stimulates $\beta 2$ -adrenergic receptors to increase skeletal muscle blood flow, glycogenolysis, and lipolysis.

(Choices C and D) Calmodulin and myosin light-chain kinase are elements of the contractile mechanism in smooth muscle, not skeletal muscle.

Educational objective:

The contractile mechanism in skeletal muscle depends on proteins (myosin II, actin, tropomyosin, and troponin) as well as calcium ions.

Physiology

Rheumatology/Orthopedics & Sports

Muscle structure & physiology

Subject

System

Topic

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order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

As part of a long-term cohort study, members of a large extended family undergo periodic analysis of multiple serum markers. Many male participants are found to have abnormal laboratory results despite no obvious signs of disease. Further analysis shows that these men have an X-linked mutation affecting the phosphoribosyl pyrophosphate (PRPP) synthetase gene, resulting in greatly increased substrate conversion.

Item 1 of 2

Which of the following organs is most likely to develop pathology secondary to this mutation?

- ☐ A. Aorta
- ☐ B. Heart
- ☐ C. Joints
- ☐ D. Liver
- ☐ E. Pancreas

As part of a long-term cohort study, members of a large extended family undergo periodic analysis of multiple serum markers. Many male participants are found to have abnormal laboratory results despite no obvious signs of disease. Further analysis shows that these men have an X-linked mutation affecting the phosphoribosyl pyrophosphate (PRPP) synthetase gene, resulting in greatly increased substrate conversion.

Item 1 of 2

Which of the following organs is most likely to develop pathology secondary to this mutation?

- ☐ A. Aorta (2%)
- ☐ B. Heart (5%)
- ☒ C. Joints (55%)
- ☐ D. Liver (33%)
- ☐ E. Pancreas (4%)

Correct

55%



01 min, 09 secs



12/19/2020

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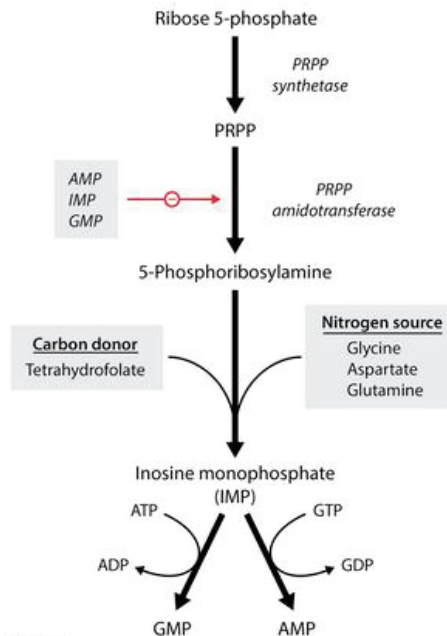
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De novo purine synthesis



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Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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Gout is a disease caused by tissue deposition of monosodium urate crystals. Elevated uric acid levels are a known risk factor for gout and increased purine metabolism is one possible cause of hyperuricemia. Phosphoribosyl pyrophosphate (PRPP) synthetase is the enzyme responsible for the production of the activated ribose necessary for de novo synthesis of purine and pyrimidine nucleotides. The mutation described in the question stem will cause increased production of purines due to feed-forward activation of the purine synthesis pathway. As a result, more purine molecules will undergo degradation, resulting in hyperuricemia and an increased risk of gout.

(Choice A) The aorta can develop aneurysms in patients with Marfan syndrome, which results from defects in fibrillin-1.

(Choices B and D) The heart and liver can be affected by glycogen storage diseases resulting from a variety of enzyme deficiencies such as glucose-6-phosphatase deficiency (von Gierke disease) and acid maltase deficiency (Pompe disease).

(Choice E) The pancreas is affected in patients with cystic fibrosis, which results from a mutation in the cystic fibrosis transmembrane conductance regulator gene. Common sequelae include pancreatitis, pancreatic insufficiency, and destruction of islet cells.



(Choice A) The aorta can develop aneurysms in patients with Marfan syndrome, which results from defects in fibrillin-1.

(Choices B and D) The heart and liver can be affected by glycogen storage diseases resulting from a variety of enzyme deficiencies such as glucose-6-phosphatase deficiency (von Gierke disease) and acid maltase deficiency (Pompe disease).

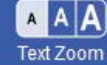
(Choice E) The pancreas is affected in patients with cystic fibrosis, which results from a mutation in the cystic fibrosis transmembrane conductance regulator gene. Common sequelae include pancreatitis, pancreatic insufficiency, and destruction of islet cells.

Educational objective:

Gout occurs with increased frequency in patients with activating mutations involving phosphoribosyl pyrophosphate synthetase due to increased production and degradation of purines.

References

- [Inherited superactivity of phosphoribosylpyrophosphate synthetase: association of uric acid overproduction and sensorineural deafness.](#)



Item 2 of 2

Incidentally, one of the male patients followed in the study is hospitalized with right knee pain and swelling. A sample of his synovial fluid shows negatively birefringent crystals under polarized light microscopy. To achieve rapid improvement in this patient's symptoms, therapy should be directed toward inhibiting which of the following types of cells?

- ☐ A. Eosinophils
- ☐ B. Lymphocytes
- ☐ C. Neutrophils
- ☐ D. Synovial cells
- ☐ E. Mast cells

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Previous



Next



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Tutorial



Lab Values



Notes



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Item 2 of 2

Incidentally, one of the male patients followed in the study is hospitalized with right knee pain and swelling. A sample of his synovial fluid shows negatively birefringent **crystals** under polarized light microscopy. To achieve rapid improvement in this patient's symptoms, therapy should be directed toward inhibiting which of the following types of cells?

- ☐ A. Eosinophils (2%)
- ☒ B. Lymphocytes (14%)
- ☐ C. Neutrophils (70%)
- ☐ D. Synovial cells (6%)
- ☐ E. Mast cells (5%)

IncorrectCorrect answer
C70%
Answered correctly01 min, 37 secs
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Acute gouty arthritis

| | |
|-----------------------------|--|
| Signs & symptoms | <ul style="list-style-type: none">Usually involves first metatarsophalangeal joint or kneeSwelling, erythema & exquisite tendernessSymptoms develop rapidly over 24 hr |
| Diagnosis | <ul style="list-style-type: none">Joint aspiration shows needle-shaped, negatively birefringent crystals |
| Treatment | <ul style="list-style-type: none">Nonsteroidal anti-inflammatory drugs (eg, naproxen, indomethacin) preferred if no contraindicationsColchicine used as second-line therapy |

This patient's synovial fluid analysis shows negatively birefringent crystals (ie, monosodium urate crystals) under polarized light, which is diagnostic for gouty arthritis. Neutrophils are the primary cells responsible for the intense inflammatory response seen in patients with gout. Phagocytosis of urate crystals by neutrophils causes the release of various cytokines and inflammatory mediators that lead to further neutrophil activation and chemotaxis, resulting in a positive feedback loop that amplifies the inflammatory response.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line therapy for treating acute gouty arthritis. They inhibit prostanoic acid biosynthesis (eg, prostaglandins, prostacyclin, thromboxanes), exerting a broad anti-





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Reverse Color



Text Zoom



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response.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line therapy for treating acute gouty arthritis. They inhibit prostanoid biosynthesis (eg, prostaglandins, prostacyclin, thromboxanes), exerting a broad anti-inflammatory effect that includes inhibition of neutrophils. Patients with contraindications to NSAIDs (eg, peptic ulcer disease, renal impairment) are often treated with colchicine, which impairs neutrophil migration and phagocytosis by interfering with microtubule formation. Colchicine also decreases tyrosine phosphorylation in response to monosodium urate crystals, resulting in decreased neutrophil activation.

(Choice A) Eosinophils function in defense against parasitic infections and are also pathogenic in patients with asthma, allergy, hypereosinophilic syndromes, and vasculitides such as Churg-Strauss syndrome.

(Choice B) Lymphocytes produce delayed-type hypersensitivity reactions that do not play a role in gout.

(Choice D) Synovial cells and macrophages play a role in initiating the inflammatory response in gouty arthritis. However, targeting these cells would not eliminate the inflammatory amplification caused by neutrophils, which is the central mechanism involved in precipitating an acute gouty attack.

(Choice E) Mast cell degranulation can be inhibited by medications such as cromolyn sodium, which is used in conditions such as asthma and allergic rhinitis.

Educational Objective:

Block Time Remaining: 00:06:05

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Feedback



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End Block



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Previous



Next



Full Screen



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Lab Values



Notes



Calculator



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Text Zoom



Settings

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(Choice E) Mast cell degranulation can be inhibited by medications such as cromolyn sodium, which is used in conditions such as asthma and allergic rhinitis.

Educational objective:

Nonsteroidal anti-inflammatory drugs (NSAIDs) are first-line therapy for treating acute gouty arthritis. They inhibit cyclooxygenase and exert a broad anti-inflammatory effect that includes inhibition of neutrophils. When NSAIDs are contraindicated (eg, peptic ulcer disease, renal impairment), colchicine is useful in the acute management of gout as it inhibits neutrophil chemotaxis and phagocytosis by preventing microtubule formation.



1



Feedback



Suspend



End Block

A 62-year-old woman comes to the office due to a 3-month history of painful, swollen wrists and knees. She also has joint stiffness, which is worse upon wakening and limits her daily activities. Review of systems is positive for fatigue. The patient's only other medical condition is hypothyroidism for which she takes levothyroxine. She smoked a pack of cigarettes daily for 20 years and quit 15 years ago. Vitals signs are within normal limits. Physical examination shows symmetric, moderate swelling of the wrists and knees. The joints are tender and warm. Range of motion is intact but painful. Plain radiographs of the symptomatic joints show joint space narrowing and marginal erosions. Which of the following cytokines are primarily involved in the pathogenesis of this patient's joint destruction?

- ☐ A. IL-1 and tumor necrosis factor-alpha
- ☐ B. IL-2 and interferon gamma
- ☐ C. IL-4 and IL-5
- ☐ D. IL-10 and transforming growth factor-beta
- ☐ E. IL-12 and IL-23



She also has joint stiffness, which is worse upon waking and limits her daily activities. Review of systems is positive for fatigue. The patient's only other medical condition is hypothyroidism for which she takes levothyroxine. She smoked a pack of cigarettes daily for 20 years and quit 15 years ago. Vitals signs are within normal limits. Physical examination shows symmetric, moderate swelling of the wrists and knees. The joints are tender and warm. Range of motion is intact but painful. Plain radiographs of the symptomatic joints show joint space narrowing and marginal erosions. Which of the following cytokines are primarily involved in the pathogenesis of this patient's joint destruction?

- ☒ A. IL-1 and tumor necrosis factor-alpha (66%)
- ☐ B. IL-2 and interferon gamma (19%)
- ☐ C. IL-4 and IL-5 (3%)
- ☐ D. IL-10 and transforming growth factor-beta (5%)
- ☐ E. IL-12 and IL-23 (4%)

Correct

66%



01 min, 11 secs



09/21/2020

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Feedback



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This patient has chronic, **symmetric, inflammatory arthritis** associated with significant **morning stiffness** and overt **synovitis** (swelling, warmth, tenderness). In association with the radiographic findings of joint space narrowing and marginal joint erosions, this presentation is typical for **rheumatoid arthritis (RA)**. RA is a progressive autoimmune disorder that has a peak incidence at age 50-75 but can occur at any age; women are affected more often than men. Systemic symptoms (eg, fatigue, fever) are common.

The pathogenesis of RA involves both humoral (eg, autoantibodies against citrullinated polypeptides) and cell-mediated immunity; activation of **CD4⁺ T cells**, especially Th1 and Th17, occurs early in the disease process. Macrophages release proinflammatory cytokines critical for the development and **progressive articular destruction** seen in RA. These include:

- **Tumor necrosis factor-alpha** (TNF-alpha) stimulates the proliferation of inflammatory cells and causes expression of inflammatory factors (eg, collagenase, prostaglandins) by synovial cells.
- **IL-1** induces synthesis of matrix metalloproteinases and enhances T-cell immune responses.

The proteases (eg, collagenase, metalloproteinase) contribute to cartilage destruction. In addition, both cytokines indirectly activate osteoclasts, resulting in bony erosions. Monoclonal antibodies that inhibit TNF-alpha (eg, adalimumab, etanercept) or IL-1 receptors (eg, anakinra) are widely used in the treatment of RA and can slow progression of the disease.

cytokines indirectly activate osteoclasts, resulting in bony erosions. Monoclonal antibodies that inhibit TNF-alpha (eg, adalimumab, etanercept) or IL-1 receptors (eg, anakinra) are widely used in the treatment of RA and can slow progression of the disease.

(Choice B) Activated Th1 cells produce significant quantities of IL-2 and interferon gamma, among other cytokines. Although Th1 cells and interferon gamma play a role in the pathogenesis of RA, IL-2 is less prominent. These cytokines are present in higher quantities in granulomatous diseases (eg, tuberculosis, sarcoidosis).

(Choice C) IL-4 and IL-5 are involved prominently in mast cell function and play a role in the pathogenesis of atopic disorders (eg, asthma).

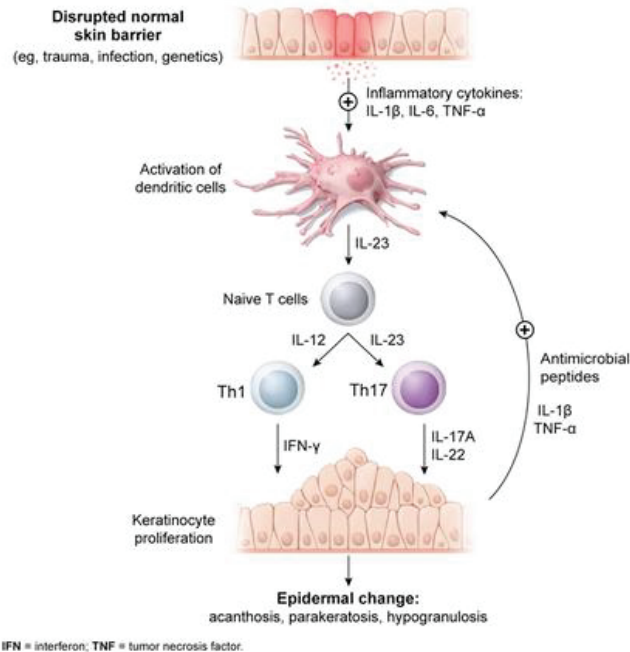
(Choice D) Transforming growth factor-beta and IL-10 are antiinflammatory cytokines that downregulate lymphocyte activation and proliferation and reduce the production of proinflammatory cytokines (eg, TNF-alpha). These cytokines are likely protective of the joint destruction seen in RA.

(Choice E) IL-12 and IL-23 are produced by activated T cells and play a prominent role in the pathogenesis of [psoriasis](#).

Educational objective:

Exhibit Display

Pathophysiology of psoriasis



(Choice C) IL-4 and IL-5 are involved prominently in mast cell function and play a role in the pathogenesis of atopic disorders (eg, asthma).

(Choice D) Transforming growth factor-beta and IL-10 are antiinflammatory cytokines that downregulate lymphocyte activation and proliferation and reduce the production of proinflammatory cytokines (eg, TNF-alpha). These cytokines are likely protective of the joint destruction seen in RA.

(Choice E) IL-12 and IL-23 are produced by activated T cells and play a prominent role in the pathogenesis of psoriasis.

Educational objective:

The pathogenesis of rheumatoid arthritis involves early activation of CD4⁺ T cells (especially Th1 and Th17 subsets) with release of cytokines such as tumor necrosis factor-alpha and IL-1 that cause destruction of cartilage and bone. Monoclonal antibodies that inhibit tumor necrosis factor-alpha or IL-1 receptors can slow progression of the disease.

References

- [Pathogenetic insights from the treatment of rheumatoid arthritis.](#)

Pathophysiology

Rheumatology/Orthopedics & Sports

Rheumatoid arthritis



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 61-year-old man comes to the office to follow up acute arthritis. He was seen at a nearby urgent care center 6 weeks ago for sudden-onset pain and swelling in the ankle. The patient was treated with an unknown analgesic with rapid relief of his pain. Since that time, his pain has resolved completely and he is now feeling well. Past medical history is notable for hypercholesterolemia, for which he takes atorvastatin. He also has a history of recurrent renal colic. On examination, his ankle appears normal with no redness, warmth, or swelling. Serum uric acid level is 9.8 mg/dL. Which of the following is the best agent for long-term management of this patient?

- ☐ A. Antibiotics
- ☐ B. Cyclooxygenase inhibitor
- ☐ C. Glucocorticoid
- ☐ D. Lipoxxygenase antagonist
- ☐ E. Uricosuric agents
- ☐ F. Xanthine oxidase inhibitor



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

center 6 weeks ago for sudden-onset pain and swelling in the ankle. The patient was treated with an unknown analgesic with rapid relief of his pain. Since that time, his pain has resolved completely and he is now feeling well. Past medical history is notable for hypercholesterolemia, for which he takes atorvastatin. He also has a history of recurrent renal colic. On examination, his ankle appears normal with no redness, warmth, or swelling. Serum uric acid level is 9.8 mg/dL. Which of the following is the best agent for long-term management of this patient?

- ☐ A. Antibiotics (0%)
- ☐ B. Cyclooxygenase inhibitor (5%)
- ☐ C. Glucocorticoid (1%)
- ☐ D. Lipoxigenase antagonist (0%)
- ☐ E. Uricosuric agents (6%)
- ☒ F. Xanthine oxidase inhibitor (85%)

Correct

85%



01 min, 05 secs



09/28/2020

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Settings

This patient had an episode of acute **gouty arthritis** that has responded to acute therapy. The decision now needs to be made whether to initiate long term preventive therapy. Patients who have only occasional episodes of gout may not need prophylactic treatment. However, uric acid-lowering medications can be helpful in patients with frequent episodes of gouty arthritis, chronic joint destruction, uric acid renal stones, or **tophi**.

In addition to acute gout, this patient has had recurring episodes of likely uric acid stones and should be considered for **prophylactic therapy**. The preferred treatment to prevent recurrent attacks is **xanthine oxidase inhibitors** (eg, allopurinol, febuxostat), which decrease uric acid production. Prophylactic therapy is usually initiated during intercritical (between attacks) periods as acute changes in serum uric acid levels can worsen an acute attack.

(Choice A) Septic arthritis can cause an acute monoarthritis but would be unlikely to respond to analgesics.

(Choice B) Nonsteroidal antiinflammatory drugs (NSAIDs) act by inhibiting cyclooxygenase. NSAIDs are the first-line therapy for acute gouty arthritis and can prevent an acute flare while urate-lowering therapy is started. However, they are not normally used for long-term therapy due to risk of peptic ulcer.

(Choice C) Oral or intraarticular glucocorticoids can be used for acute gout in patients who cannot tolerate



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Previous



Next



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Lab Values



Notes



Calculator



Reverse Color

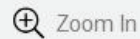
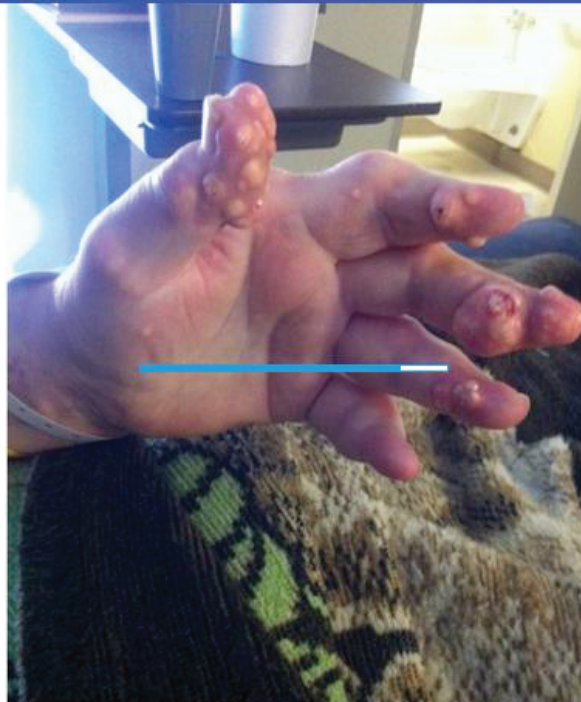


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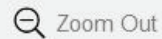


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My Notebook

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Feedback



Suspend



End Block



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Settings

analgesics.

(Choice B) Nonsteroidal antiinflammatory drugs (NSAIDs) act by inhibiting cyclooxygenase. NSAIDs are the first-line therapy for acute gouty arthritis and can prevent an acute flare while urate-lowering therapy is started. However, they are not normally used for long-term therapy due to risk of peptic ulcer.

(Choice C) Oral or intraarticular glucocorticoids can be used for acute gout in patients who cannot tolerate NSAIDs or colchicine. However, they have significant long-term side effects.

(Choice D) Lipoxxygenase inhibitors (eg, zileuton) are oral anti-inflammatory medications used in the long-term management of asthma. They are not useful for treatment of gout.

(Choice E) Uricosuric agents (eg, probenecid) are second-line drugs for chronic management of gout. These drugs increase renal excretion of uric acid and are therefore contraindicated in patients with a history of renal stones.

Educational objective:

Chronic uric acid-lowering therapy is recommended for patients with gout who have frequent gouty attacks, uric acid kidney stones, tophi, or chronic joint destruction from gout. Xanthine oxidase inhibitors are the preferred treatment.

References



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Feedback



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A group of investigators is studying osteoprotegerin function in patients with postmenopausal osteoporosis. Using an engineered mouse strain, they develop a chimeric monoclonal antibody that blocks binding of receptor activator of nuclear factor kappa B (RANK) to RANK ligand (RANK-L). The investigators inject this monoclonal antibody into human subjects. Eight weeks later, a bone biopsy is obtained from all subjects. Which of the following is the most likely observed finding?

- ☐ A. Decreased bone mineralization
- ☐ B. Decreased bone resorption
- ☐ C. Increased osteoblast activity
- ☐ D. Increased osteoclast activity
- ☐ E. Increased survival of osteocytes

Submit

A group of investigators is studying **osteoprotegerin function** in patients with postmenopausal osteoporosis. Using an engineered mouse strain, they develop a chimeric monoclonal antibody that blocks binding of receptor activator of nuclear factor kappa B (RANK) to RANK ligand (RANK-L). The investigators inject this monoclonal antibody into human subjects. Eight weeks later, a bone biopsy is obtained from all subjects. Which of the following is the most likely observed finding?

- ☐ A. Decreased bone mineralization (2%)
- ☒ B. Decreased bone resorption (80%)
- ☐ C. Increased osteoblast activity (8%)
- ☐ D. Increased osteoclast activity (6%)
- ☐ E. Increased survival of osteocytes (2%)

Correct



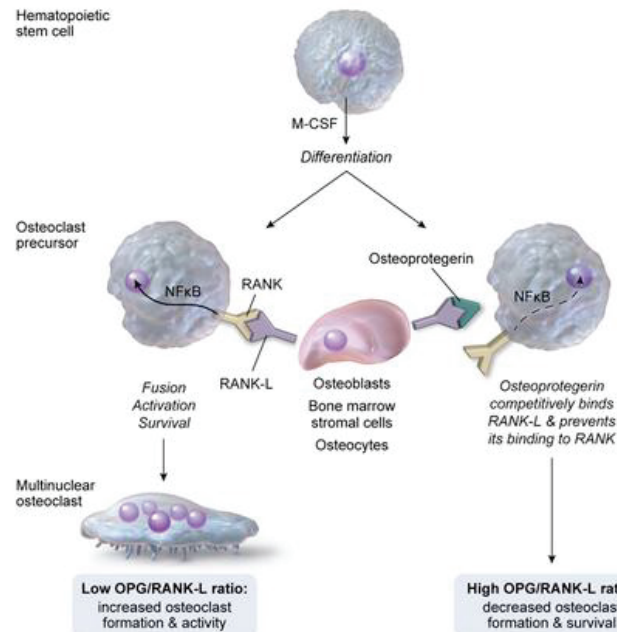
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Osteoclast differentiation



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Fusion

RANK-L

Osteoblasts

Osteoprotegerin



Mark



Previous



Next



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Lab Values



Notes



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Text Zoom



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Interaction between the receptor for activated nuclear factor kappa B (**RANK**) and its ligand (**RANK-L**), is critical for the development of mature, multinucleated osteoclasts. This **binding is blocked by osteoprotegerin** (OPG), which acts as a decoy receptor for RANK-L (preventing it from interacting with RANK). By binding RANK-L, OPG reduces the differentiation and survival of osteoclasts, resulting in decreased bone resorption and **increased bone density**.

Estrogen maintains bone mass in premenopausal women by inducing production of OPG by osteoblasts and stromal cells and decreasing expression of RANK on osteoclast precursors. The **loss of OPG at menopause** leads to increased osteoclast activity that predisposes to **osteoporosis**.

Denosumab is a monoclonal antibody used in the treatment of postmenopausal osteoporosis. It **works similar to OPG** in that it binds RANK-L and prevents its interaction with RANK receptor. Denosumab therefore causes decreased osteoclast differentiation and activity (**Choice D**) as well as **decreased bone resorption**.

(**Choices A and C**) RANK (receptor) is not present on osteoblasts, and inhibition of binding of RANK-L to RANK does not affect osteoblast activity or bone mineralization.

(**Choice E**) Osteocytes are derived from osteoblasts. Osteocyte survival is regulated by a variety of



Denosumab is a monoclonal antibody used in the treatment of postmenopausal osteoporosis. It **works**

similar to OPG in that it binds RANK-L and prevents its interaction with RANK receptor. Denosumab therefore causes decreased osteoclast differentiation and activity (**Choice D**) as well as **decreased bone resorption**.

(Choices A and C) RANK (receptor) is not present on osteoblasts, and inhibition of binding of RANK-L to RANK does not affect osteoblast activity or bone mineralization.

(Choice E) Osteocytes are derived from osteoblasts. Osteocyte survival is regulated by a variety of factors including mechanical stress, local growth factors, and steroid hormone levels. Although osteocytes produce RANK-L, which acts on osteoclasts, osteocyte survival is not dependent on the RANK signaling pathway.

Educational objective:

The nuclear factor kappa B (RANK)/RANK-ligand (RANK-L) interaction is essential for the formation and differentiation of osteoclasts. Osteoprotegerin (OPG) blocks binding of RANK-L to RANK and reduces formation of mature osteoclasts, leading to decreased bone resorption. Denosumab is a monoclonal antibody used in the treatment of postmenopausal osteoporosis that works in a manner similar to OPG.

References

A 37-year-old woman comes to the office due to left elbow discomfort and swelling for the past several days. The patient recalls no major trauma but has been participating in a high-intensity workout program recently. Physical examination findings are shown in the [exhibit](#). The patient is able to fully extend the elbow without increased pain. Pathology involving which of the following structures is the most likely cause of this patient's current condition?

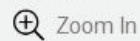
- ☐ A. Annular ligament
- ☐ B. Articular capsule
- ☐ C. Joint synovium
- ☐ D. Subcutaneous bursa
- ☐ E. Triceps tendon

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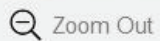
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A 37-year-old woman comes to the office due to left elbow discomfort and swelling for the past several days. The patient recalls no major trauma but has been participating in a high-intensity workout program recently. Physical examination findings are shown in the exhibit. The patient is able to fully extend the elbow without increased pain. Pathology involving which of the following structures is the most likely cause of this patient's current condition?

- ☐ A. Annular ligament (4%)
- ☒ B. Articular capsule (5%)
- ☐ C. Joint synovium (13%)
- ☒ D. Subcutaneous bursa (69%)
- ☐ E. Triceps tendon (6%)

IncorrectCorrect answer
D 69%
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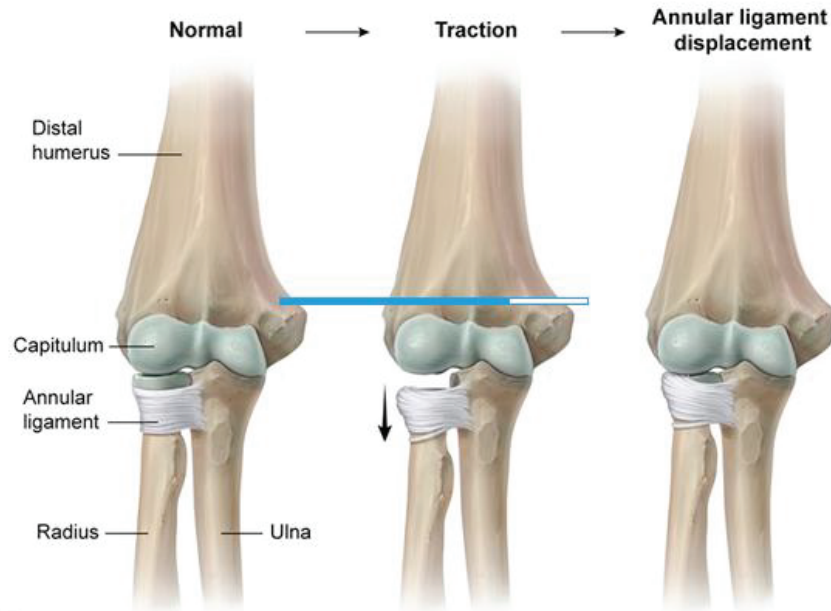
This patient has **olecranon bursitis** with **localized swelling** over the posterior elbow. The olecranon bursa is a fluid-filled **synovial sac** between the olecranon process and the skin that alleviates friction at the bony prominence. Repetitive pressure or **overuse** (eg, upper extremity exercise) can injure the bursa, leading to synovial fluid accumulation within it. Bursitis due to overuse is **noninflammatory**; associated discomfort is typically mild. However, inflammatory bursitis (eg, gout, rheumatoid arthritis, infection) can present with significant erythema and pain.

Because the bursa is **not an intraarticular structure**, bursitis typically does not interfere with joint range of motion (ie, there is **normal, pain-free range of motion**) unless it is significantly enlarged or inflamed. In contrast, intraarticular pathologies (eg, septic arthritis, intraarticular fracture) that involve the capsule, synovium, or bone impair range of motion due to joint effusion and pain; diffuse joint swelling (not localized bursal swelling) is typically present (**Choices B and C**).

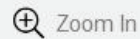
(Choice A) The annular ligament encircles the radial head and holds it and the ulna together. In children, ligamentous laxity can predispose to **radial head subluxation** (ie, nursemaid elbow) when axial traction is applied to the arm. Affected patients have mild tenderness in the anterolateral elbow (radial head) that is worsened by forearm supination. Swelling is not seen.

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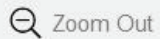
Radial head subluxation (nursemaid's elbow)



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ligamentary laxity can predispose to **radial head subluxation** (ie, nursemaid elbow) when axial traction is applied to the arm. Affected patients have mild tenderness in the anterolateral elbow (radial head) that is worsened by forearm supination. Swelling is not seen.

(Choice E) The **triceps muscle** originates from the infraglenoid tubercle of the scapula and posterior humerus and inserts onto the posterior olecranon; it extends the elbow. Triceps tendon injury leads to pain at the posterior olecranon with elbow extension, and significant swelling would be atypical.

Educational objective:

Olecranon bursitis presents with localized swelling at the olecranon process. Pain and erythema are typically minimal or absent unless significant inflammation is present. A bursa is not an intraarticular structure; therefore, range of motion of the associated joint is typically preserved and pain-free.

References

- [Common superficial bursitis.](#)

Anatomy
Subject

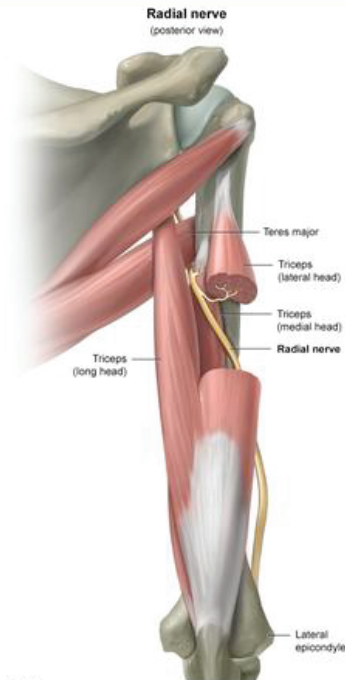
Rheumatology/Orthopedics & Sports
System

Bursitis
Topic

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ligament laxity can predispose to radial head subluxation (ie nursemaid elbow) when axial traction is

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A 6-year-old girl is brought to the office by her mother due to abdominal pain. The pain is diffuse and began this morning; it waxes and wanes in intensity. The patient has had 2 episodes of nonbilious emesis. She has had no fevers, sore throat, diarrhea, or bloody stools. Two days ago, the patient developed an erythematous, macular rash over her legs and back that has become darker and more confluent today. Blood pressure is 95/60 mm Hg. The abdomen is soft and there is diffuse, mild tenderness on palpation with no rebound, guarding, or appreciable masses. A raised, nonblanching rash is noted over the legs and back. Urinalysis results are as follows:

| | |
|--------------------|----------|
| Specific gravity | 1.022 |
| Protein | +1 |
| Blood | large |
| Glucose | negative |
| Ketones | negative |
| Leukocyte esterase | negative |
| Nitrites | negative |



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Glucose

negative

Ketones

negative

Leukocyte esterase

negative

Nitrites

negative

Which of the following renal abnormalities is most likely present in this patient?

- ☐ A. Glomerular basement membrane thickening
- ☐ B. Linear deposition of IgG on the basement membrane
- ☐ C. Localized areas of mesangial sclerosis and collapse
- ☐ D. Mesangial deposition of IgA
- ☐ E. Podocyte fusion
- ☐ F. Subepithelial immune complex deposition

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Feedback



Suspend



End Block



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Ketones negative

Leukocyte esterase negative

Nitrites negative

Which of the following renal abnormalities is most likely present in this patient?

- ☐ A. ~~Glomerular basement membrane thickening (2%)~~
- ☐ B. ~~Linear deposition of IgG on the basement membrane (6%)~~
- ☐ C. ~~Localized areas of mesangial sclerosis and collapse (3%)~~
- ☒ D. Mesangial deposition of IgA (71%)
- ☐ E. Podocyte fusion (3%)
- ☐ F. Subepithelial immune complex deposition (13%)

Correct

71%
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Henoch-Schönlein purpura (IgA vasculitis)

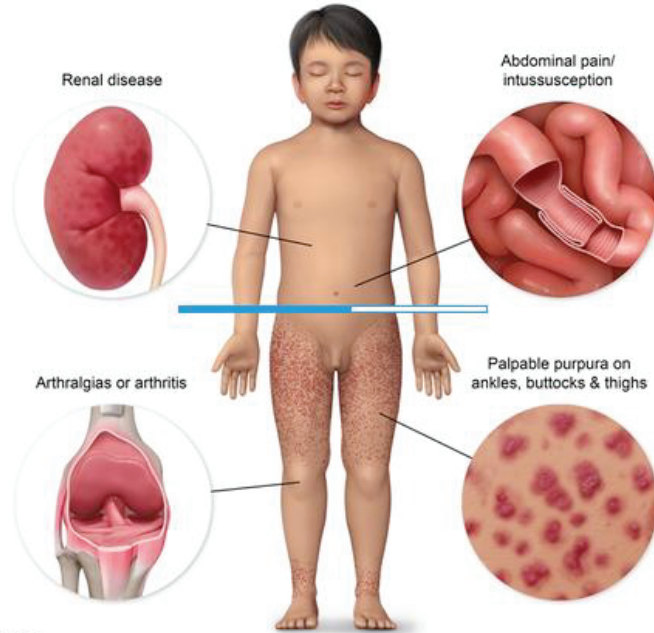
| | |
|--------------------------------|--|
| Pathogenesis | <ul style="list-style-type: none"> • Deposition of IgA in small vessels activates complement • Neutrophilic inflammation & vascular damage • Often follows an upper respiratory infection |
| Clinical manifestations | <ul style="list-style-type: none"> • Palpable purpura/petechiae on the lower extremities • Arthritis/arthralgia • Abdominal pain, gastrointestinal bleeding, intussusception • Renal disease (hematuria ± proteinuria) |
| Diagnosis | <ul style="list-style-type: none"> • Usually clinical • Skin biopsy: leukocytoclastic vasculitis, IgA deposition in vessel walls |

This patient's abdominal pain, purpura, and hematuria are consistent with **Henoch-Schönlein purpura (HSP)**, an **IgA-mediated vasculitis** of the small vessels.

The most common presenting symptom is nonblanching **palpable purpura** over the back, buttocks, and lower extremities, as seen in this patient. Colicky **abdominal pain** due to local vasculitis is also common, and other findings can include arthritis/arthralgia affecting the hips, knees, and/or ankles.

Exhibit Display

Henoch-Schönlein purpura



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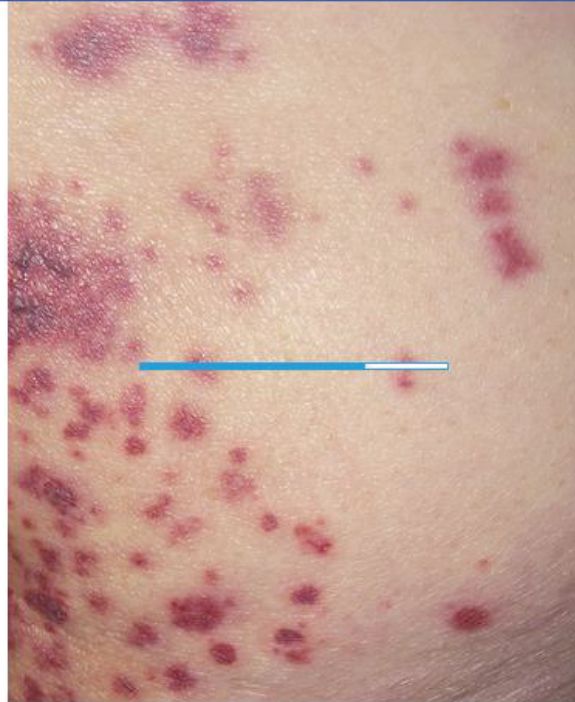
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New | Existing

My Notebook

and other findings can include **arthralgia/arthrititis** affecting the hips, knees, and/or ankles.

Renal involvement occurs in over one-third of children with HSP and is due to mesangial deposition of IgA-containing immune complexes, similar to IgA nephropathy. Most patients, especially young children, develop mild **nephritis** characterized by **hematuria**, red cell casts, and nonnephrotic-range **proteinuria**. Serum creatinine is typically normal or slightly elevated. However, more severe complications (eg, acute kidney injury) can occur in a minority of patients.

(Choice A) Membranous nephropathy is characterized by thickening of the glomerular basement membrane. It is far more common in adults than children and presents with edema and nephrotic-range proteinuria ($\geq 3+$). Moreover, purpura would not be expected.

(Choice B) Goodpasture syndrome, which typically affects adolescents and adults, is characterized by glomerulonephritis due to linear deposition of IgG antibodies on the basement membrane. Associated findings include pulmonary hemorrhage, not purpura or abdominal pain.

(Choice C) Focal segmental glomerulosclerosis typically presents with edema and proteinuria in adults and is characterized by localized regions of mesangial sclerosis and collapse on light microscopy. This patient's age and purpura make this diagnosis unlikely.

findings include pulmonary hemorrhage, not purpura or abdominal pain.

(Choice C) Focal segmental glomerulosclerosis typically presents with edema and proteinuria in adults and is characterized by localized regions of mesangial sclerosis and collapse on light microscopy. This patient's age and purpura make this diagnosis unlikely.

(Choice E) Fusion or flattening of podocytes occurs in minimal change disease, the most common form of nephrotic syndrome in children. Patients have proteinuria and edema, not hematuria and rash.

(Choice F) Subepithelial immune complex deposition is characteristic of poststreptococcal glomerulonephritis, which can present with hematuria weeks after group A *Streptococcus* (GAS) pharyngitis or skin infection (eg, impetigo). Although a blanching, erythematous, sandpaper rash can occur with GAS (ie, scarlet fever), palpable purpura is not seen.

Educational objective:

Henoch-Schönlein purpura is an IgA-mediated small vessel vasculitis that manifests with palpable purpura on the lower extremities, abdominal pain, arthralgia/arthritis, and renal disease (hematuria \pm proteinuria). Renal involvement is due to IgA deposition in the mesangium.

Pathophysiology

Rheumatology/Orthopedics & Sports

IgA vasculitis



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 70-year-old white woman is brought to the emergency department due to acute right hip pain after a fall. She was walking in her house when she tripped on a floor rug and fell, landing on her hip. The patient has been unable to bear weight on the right leg since the fall and had to call for emergency transport to the hospital. She has no significant medical history and does not use tobacco, alcohol, or illicit drugs. The patient's only medication is an over-the-counter multivitamin. Family history is notable for a hip fracture in her mother. Blood pressure is 150/90 mm Hg and pulse is 112/min. The patient is in moderate pain and her right leg appears shortened and externally rotated. There is tenderness and swelling of the right hip. Radiographs reveal a right femoral neck fracture. Which of the following changes in bone structure is most likely responsible for this patient's condition?

- ☐ A. Lamellar bone structure resembling a mosaic
- ☐ B. Osteoid matrix accumulation around trabeculae
- ☐ C. Persistence of primary spongiosa in the medullary canal
- ☒ D. Subperiosteal bone resorption and cystic degeneration
- ☐ E. Trabecular thinning with fewer interconnections



1



Feedback



Suspend



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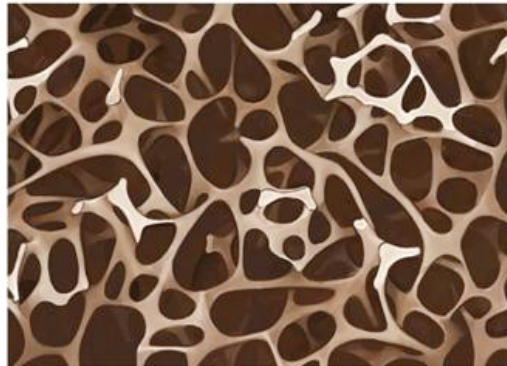
She was walking in her house when she tripped on a floor rug and fell, landing on her hip. The patient has been unable to bear weight on the right leg since the fall and had to call for emergency transport to the hospital. She has no significant medical history and does not use tobacco, alcohol, or illicit drugs. The patient's only medication is an over-the-counter multivitamin. Family history is notable for a hip fracture in her mother. Blood pressure is 150/90 mm Hg and pulse is 112/min. The patient is in moderate pain and her right leg appears shortened and externally rotated. There is tenderness and swelling of the right hip. Radiographs reveal a right femoral neck fracture. Which of the following changes in bone structure is most likely responsible for this patient's condition?

- ☐ A. Lamellar bone structure resembling a mosaic (3%)
- ☐ B. Osteoid matrix accumulation around trabeculae (3%)
- ☐ C. Persistence of primary spongiosa in the medullary canal (1%)
- ☐ D. Subperiosteal bone resorption and cystic degeneration (14%)
- ☒ E. Trabecular thinning with fewer interconnections (77%)

Normal trabecular bone



Osteoporotic bone



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This patient has a fragility fracture (ie, due to low-intensity trauma that would not cause a fracture in normal bone). In light of her white ethnicity and post-menopausal age, this is likely due to **osteoporosis**. After menopause, declining estrogen levels accelerate the loss of bone mass with a decrease in osteoblastic and an increase in osteoclastic activity. Other common risk factors include low body weight, smoking, heavy alcohol intake, and sedentary lifestyle.

The 2 major types of bone are trabecular (also called cancellous or spongy bone) and cortical. **Trabecular**



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

The 2 major types of bone are trabecular (also called cancellous or spongy bone) and cortical. **Trabecular bone** composes only 15% of the skeleton by weight but is metabolically more active due to its large surface area. Initially following menopause, bone loss predominantly affects trabecular bone, especially in the dorsolumbar vertebral bodies. Morphologic characteristics include **trabecular thinning** and perforation with **loss of interconnecting bridges**. With continued aging, cortical bone, which composes most of the appendicular skeleton, also becomes involved. The neck of the femur has components of both trabecular and cortical bone, and is a common site of osteoporotic fracture.

(Choice A) Paget disease of bone is caused by defective osteoid formation and increased bone remodeling. Collagen is laid down in a haphazard manner, resulting in a mosaic pattern of bone with irregular sections of lamellar bone linked by prominent cement lines. Paget disease typically presents with bone pain and deformity with osteolytic or mixed lytic/sclerotic lesions on x-ray.

(Choice B) Osteomalacia is commonly due to vitamin D deficiency, and is characterized by unmineralized osteoid deposits on trabecular surfaces. The bone is weak and prone to fracture, but symptomatic patients typically have bone pain, muscle weakness, and impaired ambulation.

(Choice C) Osteopetrosis is a group of disorders characterized by impaired osteoclast function. This leads to persistence of the primary spongiosa in the medullary cavity. These rare disorders typically





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



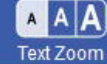
Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice C) Osteopetrosis is a group of disorders characterized by impaired osteoclast function. This leads to persistence of the primary spongiosa in the medullary cavity. These rare disorders typically present early in life with fractures, deformities, and hematologic cytopenias (due to obliteration of the marrow space).

(Choice D) Bone disease in hyperparathyroidism is characterized by increased bone resorption in cortical bone with subperiosteal thinning and cystic degeneration (osteitis fibrosa cystica). However, this is typically seen in advanced cases along with diffuse bone pain and manifestations of hypercalcemia (eg, constipation, neuropsychiatric symptoms).

Educational objective:

Initially in osteoporosis, bone loss predominantly affects trabecular bone, leading to trabecular thinning and perforation with loss of interconnecting bridges. Over time, cortical bone, which composes most of the appendicular skeleton, also becomes involved.

Pathology

Rheumatology/Orthopedics & Sports

Osteoporosis

Subject

System

Topic

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1



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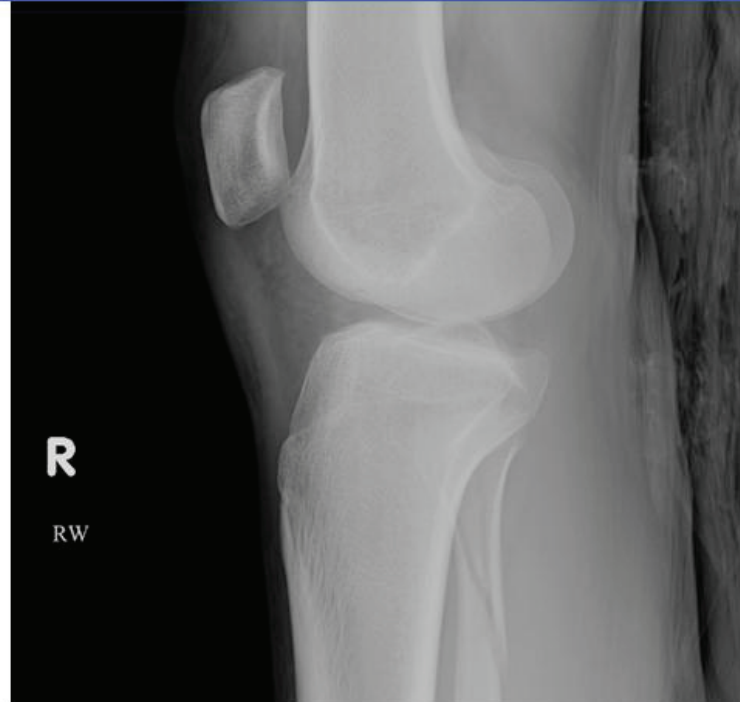


A 17-year-old boy is brought to the emergency department due to a lower extremity injury. The patient was playing football with his friends when he was tackled roughly and "felt something snap" in his right leg. He avoids bearing weight on the right foot. Examination shows a large contusion with point tenderness at the proximal lateral right leg. An x-ray of the leg is shown in the [exhibit](#). Which of the following would most likely be found on physical examination?

- ☐ A. Loss of inversion of the foot
- ☐ B. Loss of plantar flexion of the foot
- ☐ C. Loss of sensation at the dorsum of the foot
- ☐ D. Loss of sensation at the medial aspect of the leg
- ☐ E. Loss of sensation at the sole of the foot

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Exhibit Display



Zoom In

Zoom Out

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New | Existing

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A 17-year-old boy is brought to the emergency department due to a lower extremity injury. The patient was playing football with his friends when he was tackled roughly and "felt something snap" in his right leg. He avoids bearing weight on the right foot. Examination shows a large contusion with point tenderness at the proximal lateral right leg. An x-ray of the leg is shown in the exhibit. Which of the following would most likely be found on physical examination?

- ☐ A. Loss of inversion of the foot (7%)
- ☐ B. Loss of plantar flexion of the foot (12%)
- ☒ C. Loss of sensation at the dorsum of the foot (65%)
- ☐ D. Loss of sensation at the medial aspect of the leg (8%)
- ☐ E. Loss of sensation at the sole of the foot (5%)

Correct



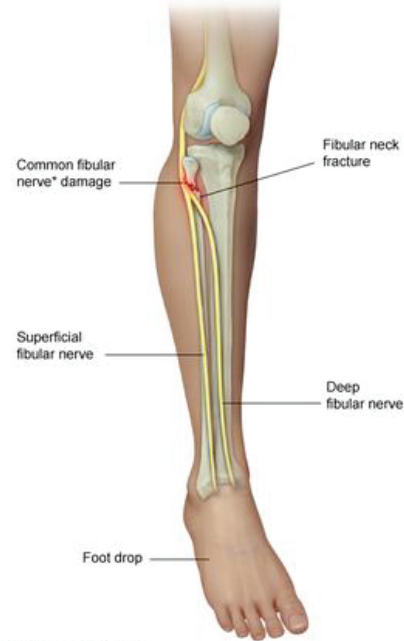
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Last Updated

Exhibit Display

Common fibular nerve injury



Zoom In Zoom Out Reset New | Existing My Notebook

fibular nerve



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

*Previously common peroneal nerve.

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The sciatic nerve branches into the **common peroneal (fibular) nerve** and the tibial nerve posteriorly in the thigh just proximal to the popliteal fossa. After coursing around the neck of the fibula, the common peroneal nerve divides into superficial and deep branches. The superficial branch innervates the muscles of the lateral compartment of the leg, which function primarily to **evert** the foot. The deep peroneal nerve innervates the anterior compartment of the leg, whose muscles act mainly as **dorsiflexors** of the foot and toes. The superficial peroneal nerve provides sensory innervation to the dorsum of the foot. The deep peroneal nerve provides sensory innervation to the region between the first and second digits of the foot.

This patient has a **fracture** of the **neck of the fibula**. The common peroneal nerve is the most frequently injured nerve in the leg due to its superficial location as it courses laterally around the neck of the fibula. Injury to the common peroneal nerve from a proximal fibula fracture would cause **loss of dorsal foot sensation** as well as impaired dorsiflexion and eversion resulting in **foot drop**.

(Choice A) The tibialis posterior (innervated by tibial nerve) is the major muscle involved in foot inversion. The tibialis anterior (innervated by common peroneal nerve) is less important, and patients with peroneal nerve injuries usually have normal foot inversion.

(Choices B and E) The **tibial nerve** courses through the popliteal fossa and innervates the skin of the



1



Feedback



Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

The tibialis anterior (innervated by common peroneal nerve) is less important, and patients with peroneal nerve injuries usually have normal foot inversion.

(Choices B and E) The **tibial nerve** courses through the popliteal fossa and innervates the skin of the posterior calf, lateral foot, and sole; tissues of the knee joint; and muscles providing plantar flexion and inversion (eg, gastrocnemius, soleus, tibialis posterior). Injury to the tibial nerve would cause weakened plantar flexion and inversion of the foot as well as decreased sensation at the sole of the foot.

(Choice D) Loss of sensation at the medial aspect of the leg would result from a lesion of the **saphenous nerve**, the largest pure sensory branch of the femoral nerve.

Educational objective:

The common peroneal nerve is vulnerable to injury where it courses around the neck of the fibula. Fibular neck fractures can injure this nerve, causing weakness of dorsiflexion (deep peroneal nerve) and eversion (superficial peroneal nerve) of the foot as well as loss of sensation over the dorsum of the foot.

Anatomy

Rheumatology/Orthopedics & Sports

Peroneal neuropathy

Subject

System

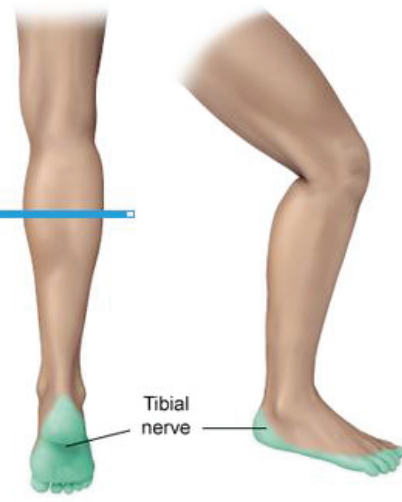
Topic

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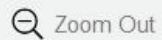
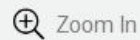
The tibialis anterior (innervated by common peroneal nerve) is less important, and patients with peroneal

Exhibit Display

Tibial nerve

| Nerve | Motor function | Cutaneous innervation |
|--------------|---|---|
| Tibial nerve | Foot plantar flexion & inversion, toe flexion |  |

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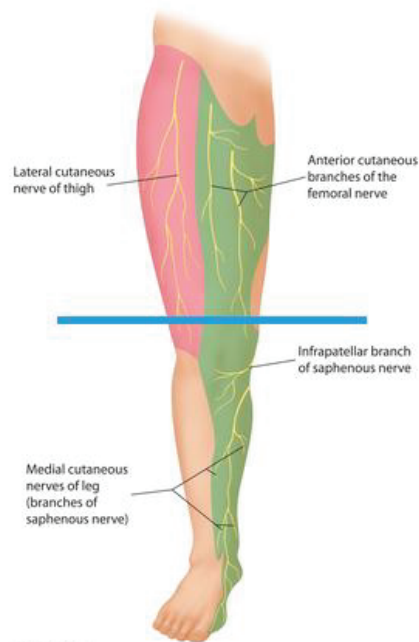
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The tibialis anterior (innervated by common peroneal nerve) is less important, and patients with peroneal

Exhibit Display

Anterior cutaneous nerves of leg



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Zoom In

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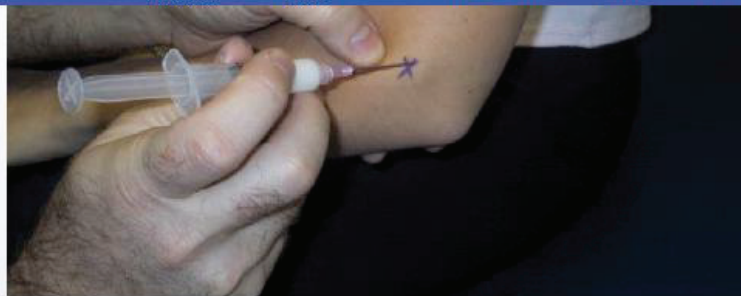
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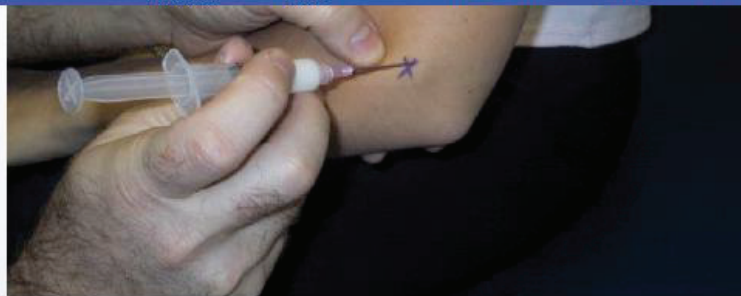
A 16-year-old girl comes to the office due to several months of left elbow pain. The pain is worse with activity and limits her exercise. She has attempted treatment with over-the-counter ibuprofen and acetaminophen but has had only partial relief. Medical history is notable for seasonal allergies, and current medications include a fluticasone nasal spray. Further evaluation shows that the patient's condition is due to a tendon injury. A long-acting glucocorticoid injection is administered at the most tender spot, as marked in the image below.





Which of the following actions is most likely performed by the affected muscle?

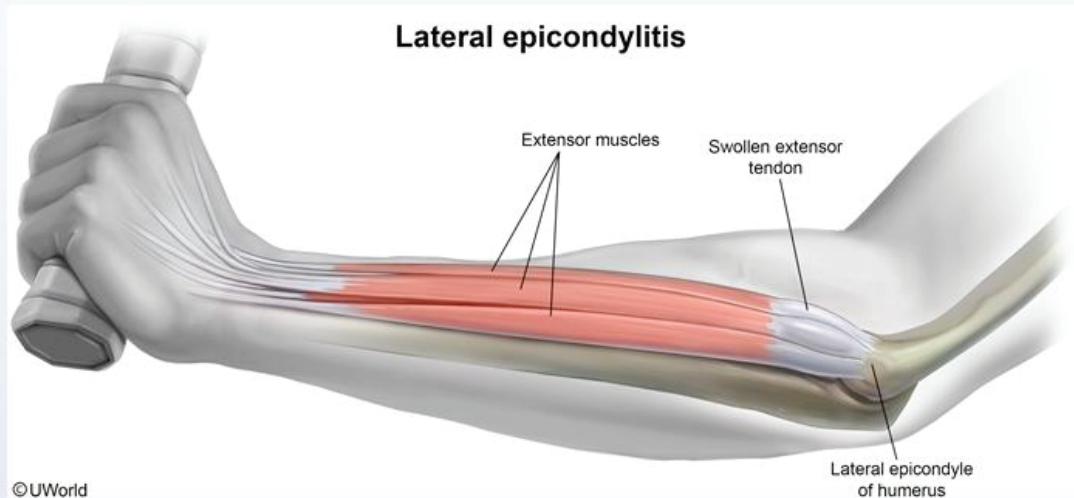
- ☐ A. Finger adduction
- ☐ B. Forearm flexion
- ☐ C. Shoulder abduction
- ☐ D. Thumb abduction
- ☐ E. Wrist extension
- ☐ F. Wrist flexion



Which of the following actions is most likely performed by the affected muscle?

- ☐ A. Finger adduction (3%)
- ☐ B. Forearm flexion (19%)
- ☐ C. Shoulder abduction (1%)
- ☐ D. Thumb abduction (3%)
- ☒ E. Wrist extension (64%)
- ☐ F. Wrist flexion (7%)

Explanation



This patient has pain over the lateral epicondyle of the humerus, suggesting **lateral epicondylitis** (ie, tennis elbow). Lateral epicondylitis is classically seen in tennis players due to repetitive **wrist extension** (backhand strikes) transmitting sudden, extreme forces through the lateral epicondyle.

The lateral epicondyle serves as the primary attachment point for **extensor carpi radialis brevis** and **extensor digitorum**, which are the primary muscles involved in wrist extension. Overuse of these muscles

(backhand strikes) transmitting sudden, extreme forces through the lateral epicondyle.

The lateral epicondyle serves as the primary attachment point for **extensor carpi radialis brevis** and **extensor digitorum**, which are the primary muscles involved in wrist extension. Overuse of these muscles can cause repetitive microtrauma of the tendons at their origins on the **lateral epicondyle**, leading to angiofibroblastic **tendinosis** (ie, excess fibroblasts and neovascularization) without a significant inflammatory infiltrate. This results in swelling and pain over the lateral epicondyle and proximal extensor tendons.

Overuse of the wrist flexor muscles can cause medial epicondylitis (ie, golfer's elbow), which occurs by a similar process in the tendons of the flexor muscles near their attachment on the medial epicondyle
(Choice F).

(Choice A) Adduction of the fingers is primarily accomplished by the palmar interosseous muscles, which originate on the metacarpals.

(Choice B) Flexion of the forearm is primarily accomplished by the biceps brachii, brachialis, and brachioradialis muscles. None of these muscles originate on the lateral epicondyle.

(Choice C) Shoulder abduction is primarily accomplished by the supraspinatus and deltoid muscles. Overuse of the supraspinatus leads to supraspinatus tendinopathy (ie, rotator cuff tendinopathy).



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice A) Adduction of the fingers is primarily accomplished by the palmar interosseous muscles, which originate on the metacarpals.

(Choice B) Flexion of the forearm is primarily accomplished by the biceps brachii, brachialis, and brachioradialis muscles. None of these muscles originate on the lateral epicondyle.

(Choice C) Shoulder abduction is primarily accomplished by the supraspinatus and deltoid muscles. Overuse of the supraspinatus leads to supraspinatus tendinopathy (ie, rotator cuff tendinopathy).

(Choice D) Overuse of the abductor pollicis longus (thumb abduction) and extensor pollicis brevis (thumb extension) can result in [de Quervain tendinopathy](#), which causes thumb and wrist pain.

Educational objective:

Lateral epicondylitis (ie, tennis elbow) is characterized by overuse of wrist extensor muscles (eg, extensor carpi radialis, extensor digitorum), leading to angiofibroblastic tendinosis at their attachment on the lateral epicondyle.

References

- [Lateral epicondylitis of the elbow.](#)



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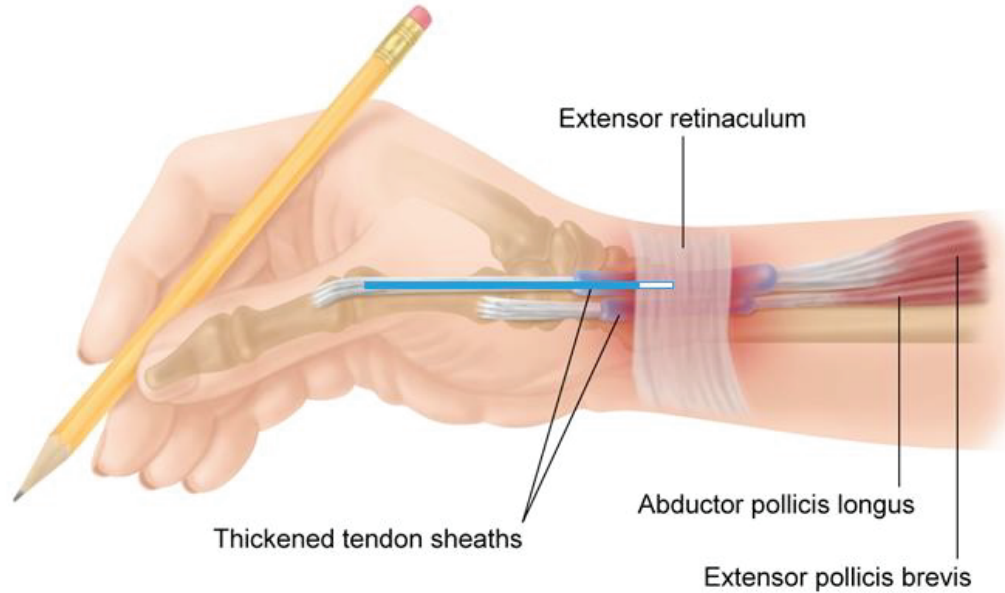
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De Quervain tendinopathy



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A 6-year-old boy has a history of 5 bone fractures, 3 of them occurring after only minimal trauma. His birth was unremarkable following a normal pregnancy. The patient has been in the 50th percentile for both height and weight since birth, and he has reached all developmental milestones. On physical examination, he is a pleasant, interactive child with small, malformed teeth. Further evaluation shows the finding in the image below.



This patient's condition is most likely associated with impairment of which of the following processes?

- ☐ A. Deposition of hyaline cartilage by chondrocytes
- ☐ B. Mineralization of osteoid into mature bone matrix



This patient's condition is most likely associated with impairment of which of the following processes?

- ☐ A. Deposition of hyaline cartilage by chondrocytes
- ☒ B. Mineralization of osteoid into mature bone matrix
- ☐ C. Osteoid production by osteoblasts
- ☐ D. Remodeling of woven bone
- ☐ E. Vascular ingrowth into epiphyseal region

Submit



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings



This patient's condition is most likely associated with impairment of which of the following processes?

- ☐ A. ~~Deposition of hyaline cartilage by chondrocytes (28%)~~
- ☒ B. ~~Mineralization of osteoid into mature bone matrix (28%)~~
- ☒ C. ~~Osteoid production by osteoblasts (29%)~~
- ☐ D. ~~Remodeling of woven bone (11%)~~
- ☐ E. ~~Vascular ingrowth into epiphyseal region (0%)~~

Incorrect

Correct answer



29%



01 min, 46 secs

Time spent



10/01/2020

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Feedback



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End Block



This child has blue sclerae and a history of **several fractures** after only **minimal trauma**. These findings are suggestive of **osteogenesis imperfecta (OI)**, a disease caused by impaired synthesis of type 1 collagen by osteoblasts. Clinical manifestations are variable and can range from mild defects to lethal disease in utero. In most patients, OI is transmitted by autosomal dominant inheritance.

Type 1 collagen is the predominant collagen in **osteoid** (organic portion of bone matrix) and allows bone to be somewhat flexible while still maintaining strength. Type 1 collagen is also present in teeth, ligaments, skin, and sclerae. In OI, deficiency of type 1 collagen causes brittle bones that are prone to fracture. Other manifestations include **blue sclerae** due to the deficient connective tissue allowing transparency of underlying vessels and **small, malformed teeth (dentinogenesis imperfecta)**. Joints can have excessive



underlying vessels and **small, malformed teeth** ([dentinogenesis imperfecta](#)). Joints can have excessive laxity, and some patients are also susceptible to bruising and hearing loss.

(Choice A) Bones are formed by endochondral ossification (eg, long bones) and intramembranous ossification (eg, flat bones). Endochondral ossification involves the deposition of hyaline cartilage by chondrocytes and is impaired in achondroplasia, which is unlikely in a patient of normal stature.

(Choice B) Bone matrix comprises inorganic (eg, hydroxyapatite crystals) and organic (eg, type 1 collagen) components. Osteoblasts release calcium-binding proteins (eg, osteocalcin) and phosphatases that promote bone mineralization. Defective mineralization of bone matrix is a characteristic feature of vitamin D deficiency.

(Choice D) Bone remodeling strengthens and repairs bone through the removal of old bone by osteoclasts and replacement with new bone by osteoblasts. Impaired remodeling leads to osteopetrosis (denser but more fragile bones). Pathologic fractures can occur, but blue sclerae are not associated with this disorder.

(Choice E) Long bones have multiple arteries that are essential for growth and maintenance. If the blood supply to the epiphysis is disrupted, the bone dies, resulting in avascular necrosis (eg, Legg-Calvé-Perthes disease). Avascular necrosis typically presents with pain and limited mobility but not pathologic fractures.

Educational objective:



underlying vessels and small, malformed teeth (dentinogenesis imperfecta). Joints can have excessive

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Zoom Out

Reset

New | Existing

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Educational objective:

Block Time Remaining: 00:17:37

TUTOR

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Feedback

Suspend

End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

collagen) components. Osteoblasts release calcium-binding proteins (eg, osteocalcin) and phosphatases that promote bone mineralization. Defective mineralization of bone matrix is a characteristic feature of vitamin D deficiency.

(Choice D) Bone remodeling strengthens and repairs bone through the removal of old bone by osteoclasts and replacement with new bone by osteoblasts. Impaired remodeling leads to osteopetrosis (denser but more fragile bones). Pathologic fractures can occur, but blue sclerae are not associated with this disorder.

(Choice E) Long bones have multiple arteries that are essential for growth and maintenance. If the blood supply to the epiphysis is disrupted, the bone dies, resulting in avascular necrosis (eg, Legg-Calvé-Perthes disease). Avascular necrosis typically presents with pain and limited mobility but not pathologic fractures.

Educational objective:

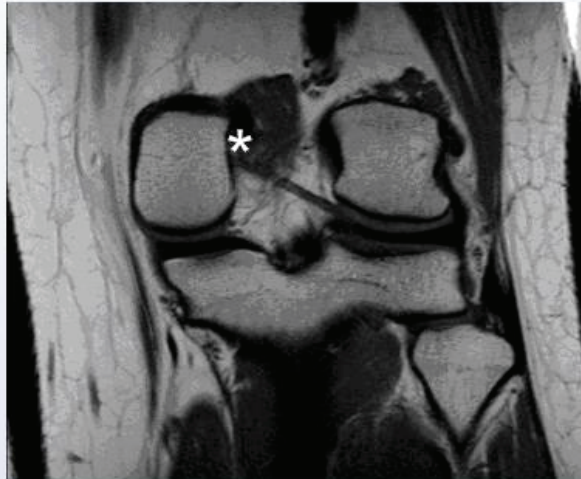
Osteogenesis imperfecta results from defective synthesis of type 1 collagen by osteoblasts. Clinical findings include a history of fractures after only minimal trauma, blue sclerae, and small, malformed teeth. In most patients, osteogenesis imperfecta is transmitted by autosomal dominant inheritance.

References

- [Osteogenesis imperfecta.](#)

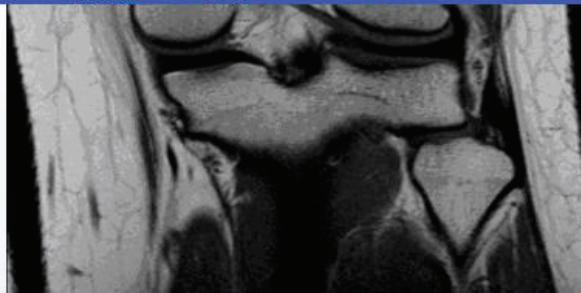


A 23-year-old athlete comes to the office with right knee pain after playing basketball. A coronal MRI of his knee viewed from the posterior aspect is shown below.



The asterisk marks the attachment site of which of the following ligaments?

- ☐ A. Anterior cruciate
- ☐ B. Patellar



The asterisk marks the attachment site of which of the following ligaments?

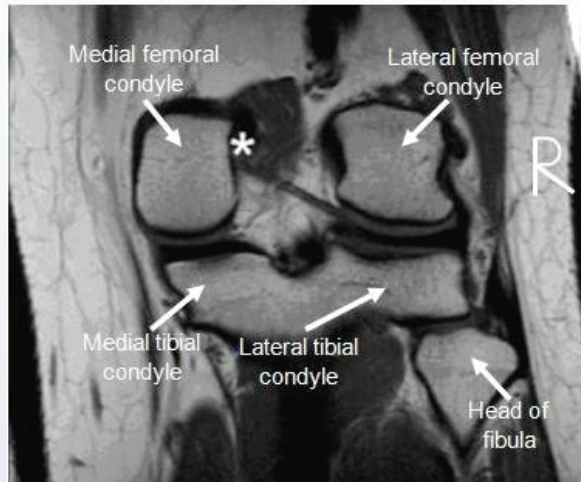
- ☐ A. Anterior cruciate
- ☐ B. Patellar
- ☐ C. Posterior cruciate
- ☐ D. Tibial collateral
- ☐ E. Transverse genicular

Submit



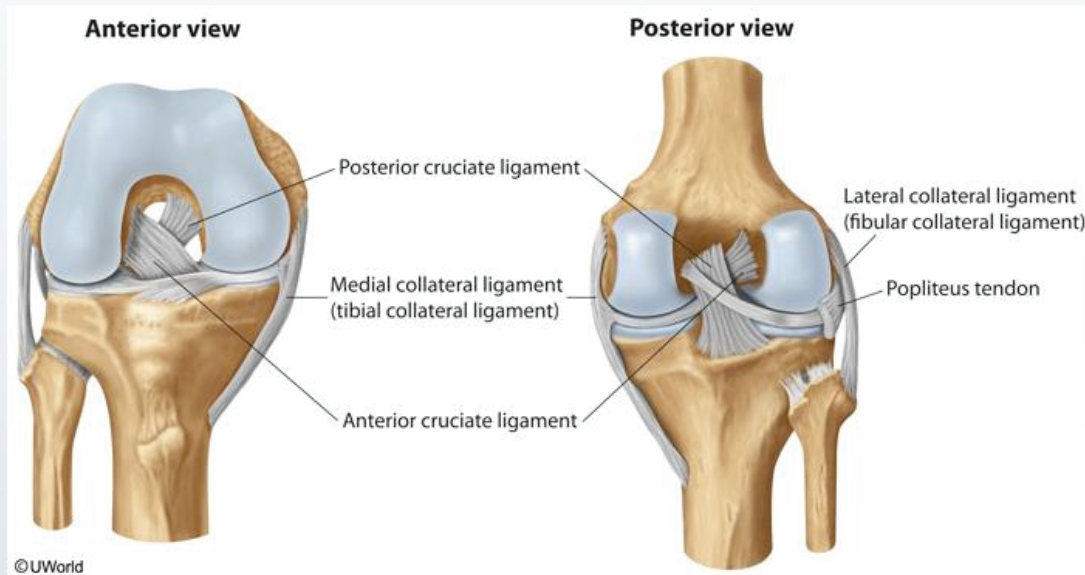
The asterisk marks the attachment site of which of the following ligaments?

- ☐ A. Anterior cruciate (36%)
- ☐ B. Patellar (0%)
- ☒ C. Posterior cruciate (58%)
- ☐ D. Tibial collateral (1%)
- ☐ E. Transverse genicular (2%)



In this coronal MRI of the right knee viewed from the posterior aspect, the opaque (white) regions, from top to bottom, correspond to the medial and lateral condyles of the femur (the medial condyle is adjacent to the asterisk), the medial and lateral condyles of the tibia, and the head of the fibula. The **anterior cruciate ligament** (ACL) and the **posterior cruciate ligament** (PCL) are located within the articular capsule of the knee joint and cross one another as each spans from the femur to the tibia. The **PCL** attaches to the posterior part of the intercondylar area of the tibia and the anterolateral surface of the medial condyle of the

posterior part of the intercondylar area of the tibia and the anterolateral surface of the medial condyle of the femur (asterisk). It prevents posterior displacement of the tibia relative to the femur when the knee is flexed (posterior drawer test).



(Choice A) The ACL is injured more commonly than the PCL. It spans from the anterior portion of the intercondylar tibia to the posterior medial side of the lateral femoral condyle. It prevents anterior



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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(Choice A) The ACL is injured more commonly than the PCL. It spans from the anterior portion of the intercondylar tibia to the posterior medial side of the lateral femoral condyle. It prevents anterior displacement of the tibia relative to the femur when the knee is flexed (anterior drawer test).

(Choice B) The patellar ligament spans from the patella to the tibial tuberosity and is the continuation of the quadriceps femoris tendon.

(Choice D) The tibial (medial) collateral ligament is a very strong band of tissue that spans from the medial femoral epicondyle to the medial condyle of the tibia. It also attaches to the medial meniscus.

(Choice E) The transverse genicular ligament attaches the medial and lateral menisci anteriorly on the proximal articular surface of the tibia.

Educational objective:

The posterior cruciate ligament prevents posterior displacement of the tibia relative to the femur when the knee is flexed. It attaches to the posterior part of the intercondylar area of the tibia and the anterior part of the lateral surface of the medial epicondyle of the femur.

Anatomy

Rheumatology/Orthopedics & Sports

Knee trauma

Subject

System

Topic

Block Time Remaining: 00:18:04

TUTOR

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1



Feedback



Suspend



End Block

A 52-year-old woman comes to the office due to worsening pain in her hands and ankles for the past several months. She also has had a nonproductive cough, anorexia, and unintentional weight loss. The patient has no prior medical conditions. Physical examination shows digital clubbing and bony tenderness affecting the wrists, hands, and ankles. There is localized right upper lung wheezing. Chest x-ray reveals an irregular mass in the peripheral right lung. Laboratory studies reveal mild normocytic anemia and normal serum electrolytes and calcium. Which of the following is the most likely cause of this patient's extremity pain?


- ☐ A. Abnormal new bone formation
- ☐ B. Avascular necrosis of bone
- ☐ C. Focal lytic bone lesions
- ☐ D. Generalized bone mineral loss

Submit

A 52-year-old woman comes to the office due to worsening pain in her hands and ankles for the past several months. She also has had a nonproductive cough, anorexia, and unintentional weight loss. The patient has no prior medical conditions. Physical examination shows digital clubbing and bony tenderness affecting the wrists, hands, and ankles. There is localized right upper lung wheezing. Chest x-ray reveals an irregular mass in the peripheral right lung. Laboratory studies reveal mild normocytic anemia and normal serum electrolytes and calcium. Which of the following is the most likely cause of this patient's extremity pain?

- ☒ A. Abnormal new bone formation (32%)
- ☐ B. Avascular necrosis of bone (6%)
- ☐ C. Focal lytic bone lesions (37%)
- ☐ D. Generalized bone mineral loss (23%)

Correct

 32%
Answered correctly 03 mins, 05 secs
Time Spent 03/05/2021
Last Updated

Hypertrophic osteoarthropathy

Clinical features

- Digital clubbing
- Joint pain
- Periostosis
- Joint effusions

Pathogenesis

- Megakaryocytes bypass lung & deposit in peripheral tissues/bone
- Focal hypoxemia & release of PDGF & VEGF
- Fibrovascular hyperplasia & abnormal bone formation

Disease associations

- Malignant: lung adenocarcinoma, metastases
- Nonmalignant lung disease (eg, cystic fibrosis, bronchiectasis, lung abscess)
- Cyanotic heart disease (right-to-left shunt)

PDGF = platelet-derived growth factor; **VEGF** = vascular endothelial growth factor.

This patient has **hypertrophic osteoarthropathy** (HOA), a syndrome characterized by painful bone and soft tissue enlargement in the distal extremities. Manifestations of HOA include **clubbing** (enlargement of



This patient has **hypertrophic osteoarthropathy** (HOA), a syndrome characterized by painful bone and soft tissue enlargement in the distal extremities. Manifestations of HOA include **clubbing** (enlargement of the distal phalanges with flattening of the nail fold), **painful arthropathy**, periostosis (tender thickening of the periosteum) of long bones, and joint effusions.

HOA commonly occurs in the setting of pulmonary malignancy, primarily **adenocarcinoma**, which characteristically arises in the lung periphery and is the most common primary lung cancer in nonsmokers. HOA can also occur with lung metastasis, certain nonmalignant lung disorders (eg, cystic fibrosis, bronchiectasis), and cyanotic heart disease.

Under normal conditions, **megakaryocytes** released from the bone marrow migrate to the pulmonary circulation, where fragmentation releases platelets into the bloodstream. However, in HOA, disruption of the normal pulmonary circulation leads to **arteriovenous shunting** and allows megakaryocytes to bypass the lungs into the systemic circulation. Upon lodging in the peripheral tissues (eg, distal digital bone), they release **platelet-derived growth factor** and **vascular endothelial growth factor**, leading to fibrovascular hyperplasia and **abnormal bone formation**.

(Choice B) Avascular necrosis (AVN) of bone is characterized by degeneration of cortical bone due to loss of arterial circulation. It usually occurs in locations that have limited or retrograde blood supply (eg, head of



hyperplasia and **abnormal bone formation**.

(Choice B) Avascular necrosis (AVN) of bone is characterized by degeneration of cortical bone due to loss of arterial circulation. It usually occurs in locations that have limited or retrograde blood supply (eg, head of femur); other than the scaphoid and lunate, it is rare in the hands and wrists. Also, this patient has no risk factors (eg, glucocorticoid use) for AVN.

(Choice C) Osteolytic skeletal metastasis is common in lung adenocarcinoma but typically affects the spine, pelvis, ribs, and long bones rather than distal limbs. Calcium is often but not always elevated.

(Choice D) Generalized bone mineral loss is characteristic of osteoporosis, which is typically painless in the absence of fracture.

Educational objective:

Hypertrophic osteoarthropathy is characterized by abnormal growth of new bone and presents with digital clubbing, painful arthropathy, periostosis of long bones, and joint effusions. It commonly occurs in the setting of pulmonary malignancy, primarily adenocarcinoma, other lung disorders (eg, cystic fibrosis, bronchiectasis), and cyanotic heart disease.

Pathology

Rheumatology/Orthopedics & Sports

Lung cancer

Subject

System

Topic



A 78-year-old woman comes to the emergency department due to acute vision loss. She had rapid-onset monocular vision loss in the left eye that developed over an hour. There is no associated pain in the eye, but the patient has had left-sided headaches most days for the last 3 weeks. She also has had achy pain in the shoulders that has slowly worsened over the last month. Examination shows decreased pupillary light reflex in the left eye with severely impaired visual acuity. Which of the following is the most appropriate treatment for this patient's condition?

- ☐ A. Acetazolamide
- ☐ B. Clopidogrel
- ☐ C. Ganciclovir
- ☐ D. Methylprednisolone
- ☐ E. Sumatriptan

Submit



A 78-year-old woman comes to the emergency department due to **acute vision loss**. She had rapid-onset monocular vision loss in the left eye that developed over an hour. There is no associated pain in the eye, but the patient has had left-sided headaches most days for the last 3 weeks. She also has had achy pain in the shoulders that has slowly worsened over the last month. Examination shows decreased pupillary light reflex in the left eye with severely impaired visual acuity. Which of the following is the most appropriate treatment for this patient's condition?

- ☐ A. Acetazolamide (10%)
- ☐ B. Clopidogrel (5%)
- ☐ C. Ganciclovir (1%)
- ☒ D. Methylprednisolone (75%)
- ☐ E. Sumatriptan (6%)

Correct



75%

Answered correctly



31 secs

Time Spent



01/31/2021

Last Updated

Block Time Remaining: 00:21:40

TUTOR

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Feedback



Suspend



End Block

Giant cell arteritis

| | |
|------------------|--|
| Symptoms | <ul style="list-style-type: none">• Systemic: fever, fatigue, malaise, weight loss• Headache• Jaw claudication• Visual disturbances (eg, ischemic optic neuropathy)• Polymyalgia rheumatica |
| Diagnosis | <ul style="list-style-type: none">• Elevated erythrocyte sedimentation rate & C-reactive protein• Temporal artery biopsy: intimal thickening, elastic lamina fragmentation, multinucleated giant cells |
| Treatment | <ul style="list-style-type: none">• Glucocorticoids |

This patient has acute, painless vision loss and unilateral headaches. This presentation is most consistent with **anterior ischemic optic neuropathy** (AION) due to **giant cell arteritis (GCA)**, also termed temporal arteritis. GCA occurs almost exclusively in patients **age >50** and is characterized by granulomatous inflammation of the media with fragmentation of the internal elastic lamina, primarily in the arteries of the head and neck. It is often associated with **polymyalgia rheumatica** (PMR), which presents with achy pain



arteritis. GCA occurs almost exclusively in patients age >50 and is characterized by granulomatous

inflammation of the media with fragmentation of the internal elastic lamina, primarily in the arteries of the head and neck. It is often associated with **polymyalgia rheumatica** (PMR), which presents with achy pain in the proximal skeletal muscles (eg, shoulders, hips).

Ocular manifestations are common in GCA and can lead to irreversible vision loss. AION is due to involvement of the ciliary arteries and causes a painless, rapidly progressive decrease in visual acuity. GCA can also cause visual symptoms due to central retinal artery occlusion, extraocular palsies, and infarcts of the visual cortex. Transient monocular vision loss (amaurosis fugax) may also be seen.

Treatment for GCA and PMR includes **systemic glucocorticoids** (eg, prednisone, methylprednisolone). However, for patients with suspected GCA, treatment should be started prior to diagnostic testing (eg, erythrocyte sedimentation rate, temporal artery biopsy) because of the risk of blindness if treatment is delayed.

(Choice A) Acetazolamide is a carbonic anhydrase inhibitor/diuretic used for treating idiopathic intracranial hypertension (ie, chronic headache and vision loss; occurs mainly in young, obese women) and angle-closure glaucoma (ie, eye pain, redness, mid-dilated pupil, and cloudy cornea). Neither condition is associated with proximal muscle pain.

(Choice B) Antihistamines (eg, cetirizine, loratadine) are indicated for patients with allergic rhinitis.



(Choice B) Antiplatelet agents (eg, aspirin, clopidogrel) are indicated for patients with amaurosis fugax (eg, transient vision loss) due to carotid atherosclerosis. However, this patient's unilateral headaches and proximal muscle pain makes GCA a more likely diagnosis.

(Choice C) Ganciclovir is used to treat cytomegalovirus retinitis, which presents with blurred vision, floaters, and photopsia (sensation of flashing lights). It occurs primarily in patients with significant immune suppression (eg, advanced AIDS).

(Choice E) Sumatriptan is used for the treatment of migraine, which can cause a variety of ocular symptoms. However, new-onset migraines are uncommon in older individuals, and this patient's other symptoms are more consistent with GCA and PMR.

Educational objective:

Ocular manifestations in giant cell arteritis (temporal arteritis) can lead to rapid, severe, and irreversible vision loss. Involvement of the ciliary arteries in GCA leads to anterior ischemic optic neuropathy, which presents with a painless, rapidly progressive decrease in visual acuity. Treatment includes systemic glucocorticoids (eg, prednisone, methylprednisolone).

References

- [Giant cell arteritis: ophthalmic manifestations of a systemic disease](#)



A 34-year-old woman comes to the physician complaining of easy fatigability. She lives alone and works as an accountant. Her menstrual cycles are regular and her last menstrual period was 2 weeks ago. She does not smoke or consume alcohol. Her blood pressure is 150/90 mm Hg and pulse is 82/min. During her physical examination, she sits up from the supine position without using her hands. Which of the following muscles contributes most to the described movement?

- ☐ A. Adductor magnus
- ☐ B. Biceps femoris, long head
- ☐ C. Gluteus medius
- ☐ D. Obturator externus
- ☐ E. Psoas major
- ☐ F. Vastus medialis

Submit



A 34-year-old woman comes to the physician complaining of easy fatigability. She lives alone and works as an accountant. Her menstrual cycles are regular and her last menstrual period was 2 weeks ago. She does not smoke or consume alcohol. Her blood pressure is 150/90 mm Hg and pulse is 82/min. During her physical examination, she sits up from the **supine position** without using her hands. Which of the following muscles contributes most to the described movement?

- ☐ A. Adductor magnus (2%)
- ☐ B. Biceps femoris, long head (5%)
- ☐ C. Gluteus medius (10%)
- ☐ D. Obturator externus (2%)
- ☒ E. Psoas major (72%)
- ☐ F. Vastus medialis (5%)

Correct

72%
Answered correctly

01 min, 04 secs
Time Spent

12/22/2020
Last Updated





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Major muscles responsible for motion at the hip

| Flexion | Extension | Abduction | Adduction |
|---|--|---|---|
| <ul style="list-style-type: none"> • Iliopsoas • Rectus femoris • Tensor fascia lata | <ul style="list-style-type: none"> • Gluteus maximus • Semitendinosus • Semimembranosus • Biceps femoris - long head | <ul style="list-style-type: none"> • Gluteus medius • Gluteus minimus | <ul style="list-style-type: none"> • Adductor brevis • Adductor longus • Adductor magnus |

Major muscles used when sitting up from the supine position include the external abdominal obliques, the rectus abdominis, and the hip flexors. The psoas major and iliacus contribute most significantly to the hip flexion; they, along with the psoas minor, are collectively known as the iliopsoas. The capacity of these muscles to carry out this motion can be deduced from the fact that they originate on the pelvis and spinal column, cross the hip joint, and insert on the femur.

The psoas major muscle arises from the bodies and intervertebral discs of the inferior-most thoracic and all of the lumbar vertebrae. The iliacus originates from the iliac fossa, a large concave surface found on the



1



Feedback



Suspend



End Block

column, cross the hip joint, and insert on the femur.

The psoas major muscle arises from the bodies and intervertebral discs of the inferior-most thoracic and all of the lumbar vertebrae. The iliacus originates from the iliac fossa, a large concave surface found on the inner aspect of the ilium. Both muscles insert via the common iliopsoas tendon into the lesser trochanter of the femur.

(Choice A) The adductor portion of the adductor magnus originates from the inferior ramus of the ischium and inserts into the proximal two-thirds of the posteromedial femur. It is a powerful adductor of the thigh.

(Choice B) The long head of the biceps femoris originates from the ischial tuberosity and inserts into the lateral head of the fibula; it functions as a thigh extensor and leg flexor.

(Choice C) The gluteus medius abducts the femur and is important in keeping the hip level during gait when the body's weight rests on one leg.

(Choice D) The obturator externus arises from the anteromedial surface of the obturator foramen and inserts near the greater trochanter of the femur. This muscle is a lateral rotator of the thigh.

(Choice F) The vastus medialis is a component of the quadriceps femoris. It arises from the proximal femur and ultimately inserts into the tibial tuberosity by means of the patella. It functions as a knee extensor.



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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(Choice F) The vastus medialis is a component of the quadriceps femoris. It arises from the proximal femur and ultimately inserts into the tibial tuberosity by means of the patella. It functions as a knee extensor.

Educational objective:

Muscles used when sitting up from the supine position include the external abdominal obliques, the rectus abdominis, and the hip flexors. The iliopsoas muscle is the most important of the hip flexors and includes the psoas major, psoas minor, and iliacus. The rectus femoris, sartorius, tensor fascia lata, and the medial compartment of the thigh also contribute to hip flexion.

Anatomy

Rheumatology/Orthopedics & Sports

Hip muscle

Subject

System

Topic

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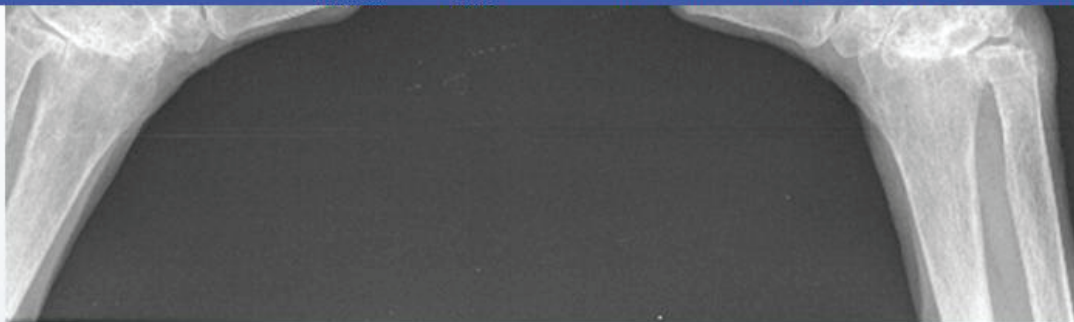
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A 61-year-old woman who recently immigrated to the United States has a long history of "joint problems." She began to have pain in her hands at age 30, and her symptoms have been intermittent but progressive since then. The symptoms were treated with nonsteroidal anti-inflammatory drugs when the pain was most severe. The patient also has a history of hypertension and chronic anemia. She does not smoke cigarettes or use illicit drugs. Family history is insignificant. On examination, there is gross deformity of multiple joints in both hands. X-ray findings are shown in the image below.





The disease process responsible for the radiographic findings would most likely affect which of the following?

- ☐ A. Cervical spine
- ☐ B. Lumbar spine
- ☐ C. Sacroiliac joints
- ☐ D. Thoracic spine

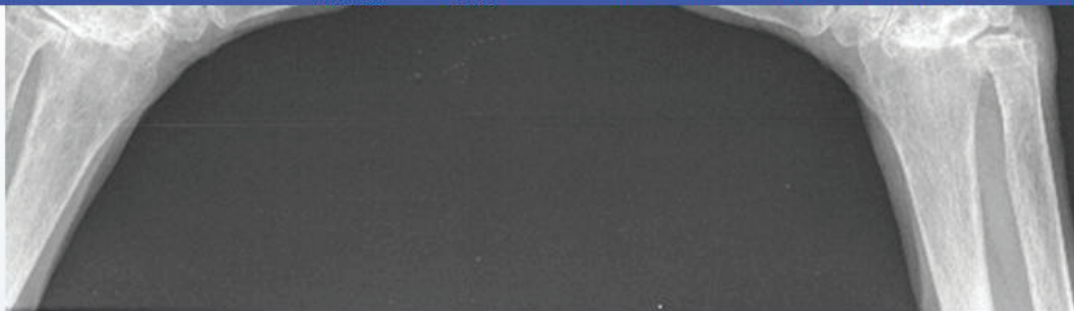
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- ☐ A. Cervical spine
- ☐ B. Lumbar spine
- ☐ C. Sacroiliac joints
- ☐ D. Thoracic spine

Submit



The disease process responsible for the radiographic findings would most likely affect which of the following?

- ✓ ☒ A. Cervical spine (46%)
- ☐ B. Lumbar spine (13%)
- ☐ C. Sacroiliac joints (33%)
- ☐ D. Thoracic spine (6%)

Correct

46%



40 secs



12/29/2020

Block Time Remaining: 00:23:24

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Feedback

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End Block

Clinical features of rheumatoid arthritis

Clinical presentation

- Pain, swelling & morning stiffness in multiple joints
- **Small joints** (PIP, MCP, MTP); spares DIP joints
- Systemic symptoms (fever, weight loss, anemia)
- **Cervical spine** involvement: subluxation, cord compression

Laboratory/imaging studies

- Positive rheumatoid factor & **anti-CCP antibodies**
- C-reactive protein & ESR correlate with disease activity
- **X-ray**: soft tissue swelling, joint space narrowing, bony erosions

Anti-CCP = anti-cyclic citrullinated peptide; **DIP** = distal interphalangeal; **ESR** = erythrocyte sedimentation rate; **MCP** = metacarpophalangeal; **MTP** = metatarsophalangeal; **PIP** = proximal interphalangeal.

This patient has chronic polyarticular arthritis, primarily involving the small joints of the hands. Her arthritis is progressive, leading to joint destruction and **ulnar deviation** of the digits, consistent with **rheumatoid arthritis (RA)**. The symptoms of RA may be relieved temporarily with nonsteroidal anti-inflammatory drugs or systemic glucocorticoids, but long-term use of disease-modifying antirheumatic drugs is recommended

is progressive, leading to joint destruction and **ulnar deviation** of the digits, consistent with **rheumatoid arthritis (RA)**. The symptoms of RA may be relieved temporarily with nonsteroidal anti-inflammatory drugs or systemic glucocorticoids, but long-term use of disease-modifying antirheumatic drugs is recommended to avoid progressive joint destruction.

In addition to the metacarpophalangeal and proximal interphalangeal joints in the hands (and metatarsophalangeal joints in the feet), RA may also involve the wrists, elbows, knees, and ankles.

Cervical spine involvement is also common in longstanding disease, and may lead to severe pain and disability due to **spinal instability** with potential radiculopathy/cord compression. The hips and lumbosacral joints are usually spared in RA.

(Choice B) The lumbar spine is only rarely involved in RA but is commonly affected by osteoarthritis.

(Choice C) Arthritis of the sacroiliac joints is characteristic of the seronegative spondyloarthropathies (ankylosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease, psoriatic arthritis). These conditions are seen most commonly in patients who carry the human leukocyte antigen B27 allele.

(Choice D) Arthritis involving the thoracic spine is uncommon and is usually due to osteoarthritis or spondyloarthritis.



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(Choice D) Arthritis involving the thoracic spine is uncommon and is usually due to osteoarthritis or spondyloarthritis.

Educational objective:

Rheumatoid arthritis causes progressive joint destruction involving the hands, wrists, elbows, and knees. Cervical spine involvement can lead to spinal instability and cord compression.

References

- [Cervical spine disease in rheumatoid arthritis: incidence, manifestations, and therapy.](#)

Pathology

Rheumatology/Orthopedics & Sports

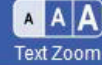
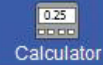
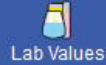
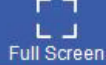
Rheumatoid arthritis

Subject

System

Topic





A 54-year-old man comes to the office due to severe foot pain. The patient attended a wedding reception where he drank several alcoholic beverages, then woke the following morning with pain. He has a long history of gouty arthritis, and his current symptoms are similar to previous flares of the disease. Past medical history includes type 2 diabetes mellitus and recently diagnosed peptic ulcer disease. Physical examination shows erythema, warmth, and swelling at the left first metatarsophalangeal joint. The patient is started on a new medication for gout that provides significant relief of his symptoms, but he returns to the clinic a week later with diarrhea and persistent nausea. The drug used in this patient most likely affects which of the following cell structures?

- ☐ A. Cytoskeleton
- ☐ B. Golgi apparatus
- ☐ C. Microsomes
- ☐ D. Nucleus
- ☒ E. Peroxisomes
- ☐ F. Rough endoplasmic reticulum



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- ☐ A. Cytoskeleton
- ☐ B. Golgi apparatus
- ☐ C. Microsomes
- ☐ D. Nucleus
- ☐ E. Peroxisomes
- ☐ F. Rough endoplasmic reticulum
- ☐ G. Smooth endoplasmic reticulum

medical history includes type 2 diabetes mellitus and recently diagnosed peptic ulcer disease. Physical

examination shows erythema, warmth, and swelling at the left first metatarsophalangeal joint. The patient is started on a new medication for gout that provides significant relief of his symptoms, but he returns to the clinic a week later with diarrhea and persistent nausea. The drug used in this patient most likely affects which of the following cell structures?

- ☒ A. Cytoskeleton (75%)
- ☐ B. Golgi apparatus (1%)
- ☐ C. Microsomes (5%)
- ☐ D. Nucleus (6%)
- ☐ E. Peroxisomes (5%)
- ☐ F. Rough endoplasmic reticulum (3%)
- ☐ G. Smooth endoplasmic reticulum (1%)

Correct

75%

51 secs

09/27/2020

Block Time Remaining: 00:24:15

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Feedback

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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The preferred first-line treatment for acute gouty arthritis is a nonsteroidal anti-inflammatory drug, but these are contraindicated in patients with a recent history of peptic ulcer. Other treatment options include colchicine and oral or intraarticular glucocorticoids.

Colchicine binds to the intracellular protein **tubulin** and inhibits its polymerization into microtubules. This, in turn, disrupts cytoskeletal-dependent functions such as chemotaxis and phagocytosis. Colchicine is administered initially at the first signs of a gout flare and can be repeated an hour later. It may also be used for prophylaxis while initiating urate-lowering therapy (eg, allopurinol). Important adverse effects of colchicine include nausea, abdominal pain, and **diarrhea**, which are most common at higher doses. Colchicine should be avoided in patients who are elderly or have severe renal dysfunction.

Educational objective:

Colchicine inhibits tubulin polymerization into microtubules and can be used for acute treatment and prophylaxis of gout. Important side effects of colchicine include nausea, abdominal pain, and diarrhea.

References

- [Colchicine for acute gout.](#)

Pharmacology

Rheumatology/Orthopedics & Sports

Gout

Block Time Remaining: 00:24:15

TUTOR

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Feedback



Suspend



End Block

A 67-year-old man comes to the office due to slowly worsening pain in both legs. He has had no trauma, fever, or chills. The pain is deep and aching, is present throughout the day, and increases with weight bearing. Vital signs are normal. Examination shows bilateral bowing of the legs with palpable warmth over the anterior shins but no redness. The remainder of the examination shows no abnormalities. Imaging studies reveal bone expansion, with cortical and trabecular thickening affecting both the tibia and fibula. Which of the following patterns of serum laboratory values is most likely in this patient?

- | | Calcium | Phosphorus | Alkaline phosphatase |
|--------------------------|---------|------------|----------------------|
| <input type="radio"/> A. | Normal | Normal | Normal |
| <input type="radio"/> B. | ↑ | Normal | Normal |
| <input type="radio"/> C. | ↑ | ↑ | Normal |
| <input type="radio"/> D. | ↑ | ↑ | ↑ |
| <input type="radio"/> E. | Normal | Normal | ↑ |
| <input type="radio"/> F. | Normal | ↓ | ↑ |

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| | Calcium | Phosphorus | Alkaline phosphatase |
|--------------------------|---------|------------|----------------------|
| <input type="radio"/> A. | Normal | Normal | Normal |
| <input type="radio"/> B. | ↑ | Normal | Normal |
| <input type="radio"/> C. | ↑ | ↑ | Normal |
| <input type="radio"/> D. | ↑ | ↑ | ↑ |
| <input type="radio"/> E. | Normal | Normal | ↑ |
| <input type="radio"/> F. | Normal | ↓ | ↑ |
| <input type="radio"/> G. | ↓ | ↓ | ↑ |

Submit

Block Time Remaining: 00:24:22

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Feedback

Suspend

End Block

studies reveal **bone expansion**, with cortical and **trabecular thickening** affecting both the tibia and fibula.

Which of the following patterns of serum laboratory values is most likely in this patient?

| | Calcium | Phosphorus | Alkaline phosphatase | |
|-------------------------------------|---------|------------|----------------------|-------|
| <input type="radio"/> A. | Normal | Normal | Normal | (7%) |
| <input type="radio"/> B. | ↑ | Normal | Normal | (1%) |
| <input type="radio"/> C. | ↑ | ↑ | Normal | (2%) |
| <input type="radio"/> D. | ↑ | ↑ | ↑ | (12%) |
| <input checked="" type="radio"/> E. | Normal | Normal | ↑ | (44%) |
| <input type="radio"/> F. | Normal | ↓ | ↑ | (5%) |
| <input type="radio"/> G. | ↓ | ↓ | ↑ | (24%) |

Correct



44%

Answered correctly



01 min, 27 secs

Time Spent



03/08/2021

Last Updated

Block Time Remaining: 00:25:42

TUTOR

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Feedback



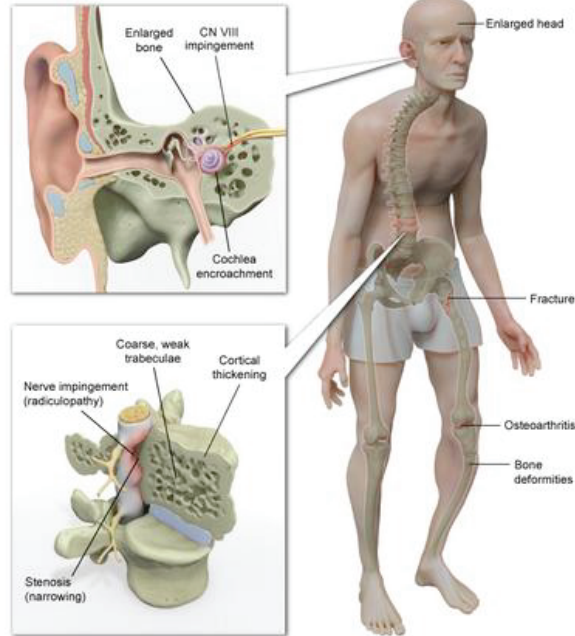
Suspend



End Block

Exhibit Display

Clinical features of Paget disease of bone



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New | Existing

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



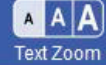
Notes



Calculator



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This patient with skeletal pain, deformity (ie, bowing of the legs), and focal warmth has **Paget disease of bone** (osteitis deformans). Paget disease is a chronic disorder characterized by excessive and disordered bone formation. The affected bone becomes **weakened**, which can lead to **bone pain, bowing**, fracture, or arthritis of adjacent joints. Increased blood flow in pagetic lesions can be apparent as **local warmth** or bruits and can occasionally lead to high-output heart failure.

Patients with Paget disease frequently have an **elevated serum alkaline phosphatase** level due to increased formation of new bone. However, **calcium, phosphorus, and parathyroid hormone levels are normal**, as calcium homeostasis remains intact by the disease process. X-rays are usually diagnostic, showing mixed lytic-sclerotic lesions, **thickening of cortical and trabecular bone**, and bony deformities.

Educational objective:

Paget disease of bone is characterized by disordered bone formation. Involvement of long bones can lead to bone pain, bowing, fracture, or arthritis of adjacent joints. Serum alkaline phosphatase is elevated due to increased production of new bone, but calcium and phosphorus levels remain normal.

References

- [Adult Paget's disease of bone: a review](#)



A 19-year-old man is brought to the emergency department after he punched through a plate glass window with his right arm. Initially there was profuse bleeding, but it stopped after direct pressure was maintained by emergency medical personnel. A deep laceration is present at the proximal aspect of the right cubital fossa, just lateral to the medial epicondyle. Examination reveals absent sensation in the lateral palm and the palmar surfaces of the first 3½ fingers, inability to flex the proximal interphalangeal joints, and inability to pronate the forearm. Additional injury to which of the following structures was most likely responsible for this patient's bleeding?

- ☐ A. Anterior interosseous artery
- ☐ B. Brachial artery
- ☐ C. Deep brachial artery
- ☐ D. Radial artery
- ☐ E. Radial recurrent artery
- ☐ F. Ulnar artery

with his right arm. Initially there was profuse bleeding, but it stopped after direct pressure was maintained by emergency medical personnel. A deep laceration is present at the proximal aspect of the right cubital fossa, just lateral to the medial epicondyle. Examination reveals absent sensation in the lateral palm and the palmar surfaces of the first 3½ fingers, inability to flex the proximal interphalangeal joints, and inability to pronate the forearm. Additional injury to which of the following structures was most likely responsible for this patient's bleeding?

- ☐ A. Anterior interosseous artery (4%)
- ☒ B. Brachial artery (53%)
- ☐ C. Deep brachial artery (10%)
- ☐ D. Radial artery (16%)
- ☐ E. Radial recurrent artery (2%)
- ☐ F. Ulnar artery (11%)

Correct

53%

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12/22/2020

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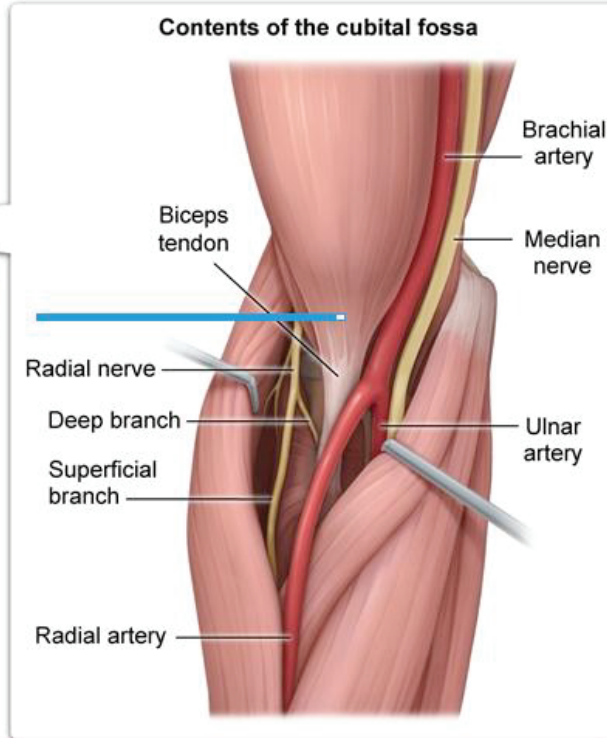
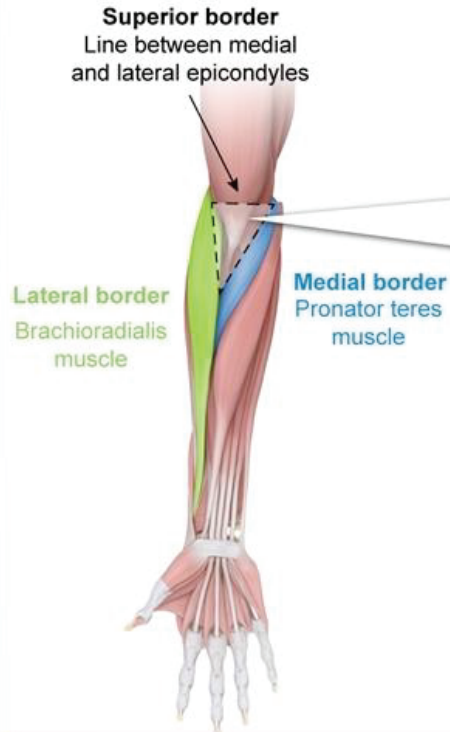
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Cubital fossa



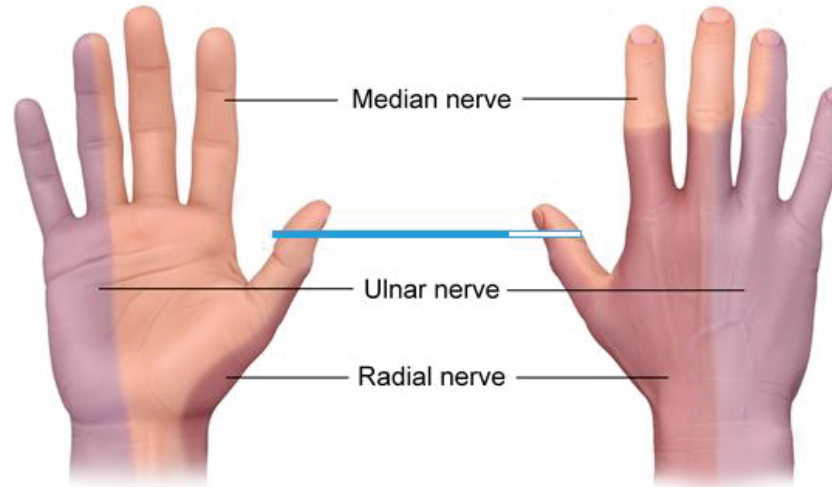
This patient's **cubital fossa laceration** has resulted in **median nerve injury**, leading to impairment of forearm pronation (pronator teres) and proximal interphalangeal joint flexion (flexor digitorum superficialis), along with sensory deficits in the **median distribution**. Because the **brachial artery is adjacent** to the median nerve at the cubital fossa, injury to the brachial artery was most likely responsible for this patient's bleeding.

The brachial artery is the **continuation** of the axillary artery as it extends past the inferior border of the teres major muscle. In the upper arm, the brachial artery courses in the medial bicipital groove between the biceps brachii and triceps brachii muscles, giving off multiple branches (eg, deep brachial artery) and running alongside both the median and ulnar nerves. Proximal to the elbow, the median and ulnar nerves diverge; **only the median nerve accompanies the brachial artery** through the **cubital fossa** (lateral to the medial epicondyle) into the proximal anterior forearm, where the brachial artery splits into the radial and ulnar arteries. In contrast, the ulnar nerve travels posterior to the medial epicondyle.

(Choice A) The **anterior interosseous artery** runs alongside the anterior interosseous nerve, a branch of the median nerve that supplies most of the deep volar forearm muscles. The anterior interosseous nerve and artery originate in the forearm, distal to the cubital fossa.

Exhibit Display

Cutaneous innervation of the hand



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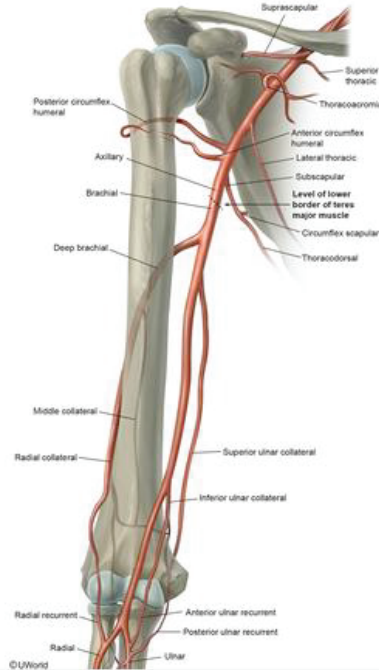
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Exhibit Display

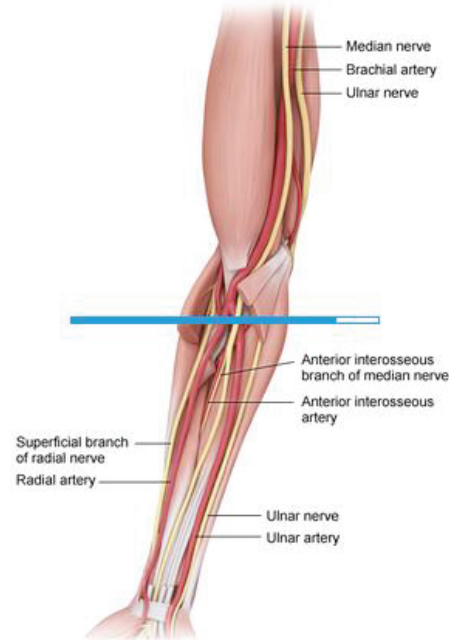
Arteries of the upper limb



Zoom In Zoom Out Reset New | Existing My Notebook

Exhibit Display

Nerves and arteries of the upper extremity



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and artery originate in the forearm, distal to the cubital fossa.

(Choice C) The **deep brachial artery** is the first branch off the brachial artery in the upper arm. It courses posterior to the humerus and is vulnerable to injury with humeral shaft fractures.

(Choices D and E) Shortly after originating from the brachial artery in the forearm, the radial artery gives off the **radial recurrent artery**, which ascends in proximity to the radial nerve near the *lateral* epicondyle. The **radial artery** then accompanies the superficial branch of the radial nerve through most of the forearm. The absence of radial nerve deficits and laceration location (cubital fossa near *medial* epicondyle) make injury to these vessels unlikely.

(Choice F) The **ulnar artery** originates from the brachial artery in the forearm (distal to the medial epicondyle). It runs alongside the ulnar nerve through most of the forearm.

Educational objective:

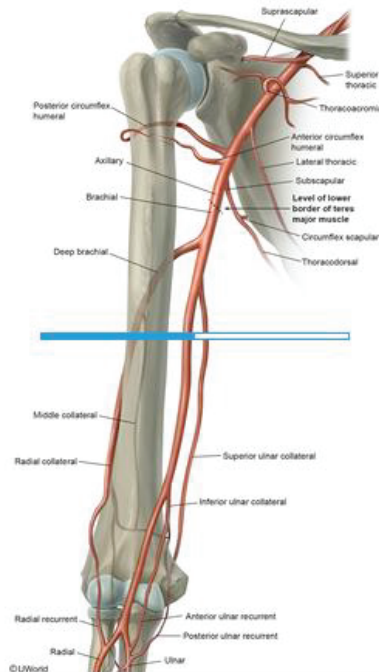
The brachial artery runs alongside the median and ulnar nerves in the medial bicipital groove of the upper arm. Proximal to the elbow, the median and ulnar nerves diverge, and the brachial artery continues with the median nerve through the cubital fossa. Injury to the median nerve at the cubital fossa frequently injures the brachial artery.

References

and artery originate in the forearm, distal to the cubital fossa.

Exhibit Display

Arteries of the upper limb



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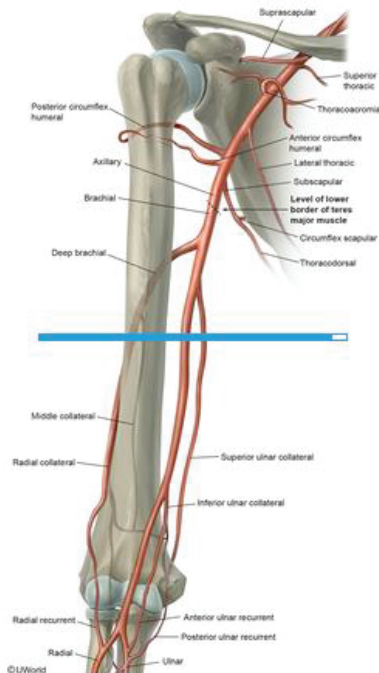
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and artery originate in the forearm, distal to the cubital fossa.

Exhibit Display

Arteries of the upper limb



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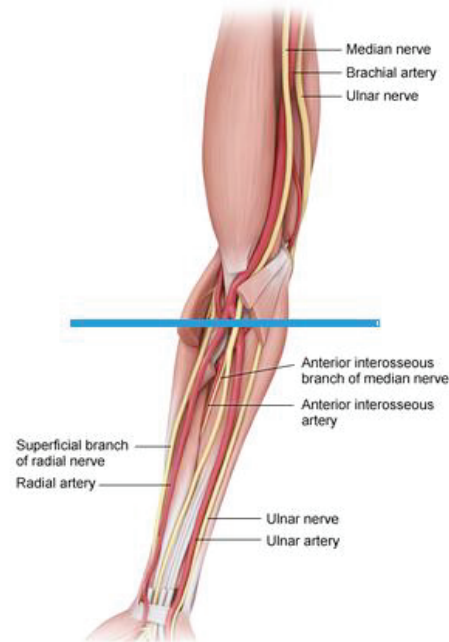
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and artery originate in the forearm, distal to the cubital fossa.

Exhibit Display

Nerves and arteries of the upper extremity



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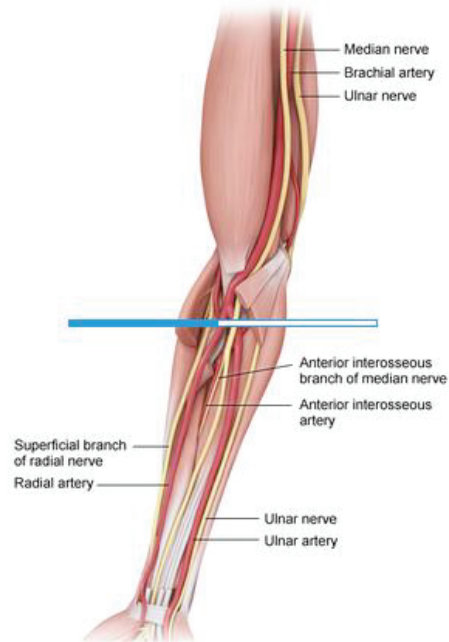
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and artery originate in the forearm, distal to the cubital fossa.

Exhibit Display

Nerves and arteries of the upper extremity



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A 44-year-old man comes to the emergency department due to worsening abdominal pain and vomiting. The patient has had 3 months of fatigue, mild abdominal pain, low-grade fever, and joint pains. On examination, the abdomen is diffusely tender to palpation with rigidity and rebound. Urgent laparotomy reveals bilateral renal infarcts and multiple segments of necrosis and perforation in the small bowel. Microscopic examination of the vessel walls shows diffuse inflammation of the adventitia and marked thickening of the inner layers due to proliferation of loose connective tissue; the arterial lumen is significantly narrowed. Which of the following is the most likely diagnosis?

- ☐ A. Bacterial endocarditis
- ☐ B. Granulomatosis with polyangiitis
- ☐ C. Inherited thrombophilia
- ☐ D. Polyarteritis nodosa
- ☐ E. Thromboangiitis obliterans

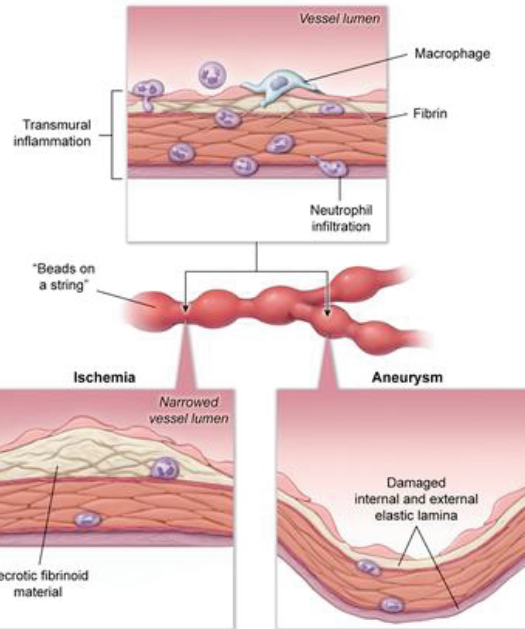
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A 44-year-old man comes to the emergency department due to worsening abdominal pain and vomiting. The patient has had 3 months of fatigue, mild abdominal pain, low-grade fever, and joint pains. On examination, the abdomen is diffusely tender to palpation with rigidity and rebound. Urgent laparotomy reveals bilateral renal infarcts and multiple segments of necrosis and perforation in the small bowel. Microscopic examination of the vessel walls shows diffuse inflammation of the adventitia and marked thickening of the inner layers due to proliferation of loose connective tissue; the arterial lumen is significantly narrowed. Which of the following is the most likely diagnosis?

- ☐ A. Bacterial endocarditis (1%)
- ☐ B. Granulomatosis with polyangiitis (13%)
- ☐ C. Inherited thrombophilia (1%)
- ☒ D. Polyarteritis nodosa (70%)
- ☐ E. Thromboangiitis obliterans (13%)

Exhibit Display

Polyarteritis nodosa



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This patient's systemic symptoms, renal/small-bowel infarctions, and biopsy findings are consistent with **polyarteritis nodosa (PAN)**, a systemic vasculitis of **medium-sized muscular arteries**. PAN is generally marked by the following:

- Segmental, transmural inflammation of the arterial wall with invasion of neutrophils and monocytes
- Destruction of the inner portion of the arterial wall; the normal architecture is replaced with **necrotic fibrinoid material** and **loose connective tissue**, which **narrows the vessel lumen** and increases the risk of **thrombosis** and tissue infarction.
- Destruction of the internal and external elastic laminae, which increases the risk of **microaneurysms** and subsequent rupture

Patients with PAN generally present with weeks or months of nonspecific **constitutional symptoms** (eg, weight loss, fatigue, low-grade fever, arthralgias) and signs of tissue ischemia in the kidneys (eg, **renal infarction**), gastrointestinal tract (eg, **small-bowel infarction**, mesenteric ischemia), peripheral nerves, and/or skin. Because PAN is not associated with antineutrophilic cytoplasmic antibodies or significant elevation in antinuclear antibodies, diagnostic confirmation usually requires tissue biopsy.

(Choices A and C) Bacterial endocarditis can cause embolic septic infarctions in the kidneys and





(Choices A and C) Bacterial endocarditis can cause embolic septic infarctions in the kidneys and intestines. Inherited coagulation disorders can also cause thrombosis with tissue infarctions. However, biopsy would show a clot/embolism in the arterial lumen (during acute infarction), not transmural inflammation and connective tissue proliferation.

(Choice B) Granulomatosis with polyangiitis usually causes manifestations in the upper/lower airways (eg, rhinosinusitis, hemoptysis) and kidneys (eg, glomerulonephritis). The gastrointestinal tract is not typically affected. Furthermore, biopsy generally reveals a leukocytoclastic vasculitis with minimal or no luminal narrowing or fibrinoid necrosis.

(Choice E) Thromboangiitis obliterans occurs primarily in young smokers. It is marked by inflammatory thrombi in the small- and medium-sized vessels of the extremities. Patients usually have digital ulcers, ischemia, gangrene, or limb claudication. Mesenteric and renal infarction would be atypical. In addition, transmural inflammation/connective tissue proliferation would not be seen during the acute stage of infarction.

Educational objective:

Polyarteritis nodosa is a systemic vasculitis of medium-sized muscular arteries marked by segmental, transmural, arterial wall inflammation with fibrinoid necrosis. This narrows the arterial lumen and increases



affected. Furthermore, biopsy generally reveals a leukocytoclastic vasculitis with minimal or no luminal narrowing or fibrinoid necrosis.

(Choice E) Thromboangiitis obliterans occurs primarily in young smokers. It is marked by inflammatory thrombi in the small- and medium-sized vessels of the extremities. Patients usually have digital ulcers, ischemia, gangrene, or limb claudication. Mesenteric and renal infarction would be atypical. In addition, transmural inflammation/connective tissue proliferation would not be seen during the acute stage of infarction.

Educational objective:

Polyarteritis nodosa is a systemic vasculitis of medium-sized muscular arteries marked by segmental, transmural, arterial wall inflammation with fibrinoid necrosis. This narrows the arterial lumen and increases risk of thrombosis and tissue ischemia/infarction. Damage to the internal and external elastic laminae also increases the risk of microaneurysm. Tissue damage primarily occurs in the kidneys, gastrointestinal tract, neurologic system, and skin; the lungs are usually spared.

Pathology

Rheumatology/Orthopedics & Sports

Polyarteritis nodosa

Subject

System

Topic

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Previous



Next



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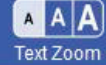
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A 45-year-old woman comes to the office due to gradually progressive pain, stiffness, and swelling of her hand joints for the past several months. The patient has had prolonged morning stiffness and significant restriction of her daily activities due to the pain, as well as generalized fatigue. She describes the symptoms over the last several weeks as "disabling," and she needs assistance with activities of daily living in the morning. The patient has tried over-the-counter pain medications, such as acetaminophen and ibuprofen, with only minimal relief of her symptoms. She has no other medical problems. Family history is significant for diabetes mellitus on her maternal side. Which of the following drugs would provide the most rapid relief of her symptoms?

- ☐ A. Colchicine
- ☐ B. Hydroxychloroquine
- ☐ C. Methotrexate
- ☐ D. Minocycline
- ☐ E. Prednisone
- ☐ F. Sulfasalazine



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restriction of her daily activities due to the pain, as well as generalized fatigue. She describes the symptoms over the last several weeks as "disabling," and she needs assistance with activities of daily living in the morning. The patient has tried over-the-counter pain medications, such as acetaminophen and ibuprofen, with only minimal relief of her symptoms. She has no other medical problems. Family history is significant for diabetes mellitus on her maternal side. Which of the following drugs would provide the most rapid relief of her symptoms?

- ☐ A. Colchicine (7%)
- ☐ B. Hydroxychloroquine (2%)
- ☐ C. Methotrexate (23%)
- ☐ D. Minocycline (0%)
- ☒ E. Prednisone (63%)
- ☐ F. Sulfasalazine (3%)

Correct

63%



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01/15/2021

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This patient has swelling, pain, and morning stiffness in multiple joints for >6 weeks, consistent with **rheumatoid arthritis (RA)**. The foundation of management for RA is **disease-modifying antirheumatic drugs (DMARDs)**, which alleviate pain and inflammation and reduce long-term **joint destruction** and disability. Examples of DMARDs are methotrexate (typically first-line), sulfasalazine, hydroxychloroquine, minocycline, and tumor necrosis factor-alpha inhibitors.

However, the response to DMARD therapy typically takes weeks (**Choices B, C, D, and F**). Therefore, short-term treatment with anti-inflammatory therapies, including systemic and intraarticular **glucocorticoids** (eg, prednisone) or **nonsteroidal anti-inflammatory drugs (NSAIDs)**, can provide rapid, temporary relief of symptoms in patients starting on DMARDs. However, they do not provide adequate long-term control of disease or prevention of joint deformity.

Glucocorticoids exert their anti-inflammatory effects by inhibiting phospholipase A2, which decreases prostaglandin and leukotriene synthesis. Glucocorticoids also depress the immune response by inhibiting the transcription of multiple cytokines and adhesion proteins, which reduces leukocyte recruitment and activation.

(Choice A) Colchicine is used in the management of both acute and chronic gout. Colchicine works by binding to tubulin and inhibiting microtubule polymerization. This results in disruption of neutrophil



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Previous



Next



Full Screen



Tutorial



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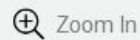


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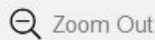


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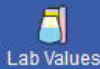
Next



Full Screen



Tutorial



Lab Values



Notes



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activation.

(Choice A) Colchicine is used in the management of both acute and chronic gout. Colchicine works by binding to tubulin and inhibiting microtubule polymerization. This results in disruption of neutrophil chemotaxis and phagocytosis, thereby reducing the inflammatory response to uric acid crystals. Colchicine is not effective in RA.

Educational objective:

The foundation of management for rheumatoid arthritis is disease-modifying antirheumatic drugs, which alleviate pain and inflammation and reduce long-term joint destruction. However, the response to treatment may take several weeks. Nonsteroidal anti-inflammatory drugs and glucocorticoids can provide rapid symptom relief in the interim.

References

- [Efficacy of prednisone 1-4 mg/day in patients with rheumatoid arthritis: a randomised, double-blind, placebo controlled withdrawal clinical trial.](#)

Pharmacology

Rheumatology/Orthopedics & Sports

Rheumatoid arthritis

Subject

System

Topic

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A 34-year-old man comes to the physician reporting one week of inability to extend his right wrist and several of his fingers on the same hand. He first began having difficulty while trying to type his thesis for graduate school on his computer. He is right-handed and does not recall any trauma. He has a history of asthma that was diagnosed while he was in college. Physical examination demonstrates impaired dorsiflexion of the right wrist with normal strength of the left wrist. Laboratory studies show:

Complete blood count

Hemoglobin 13 g/dL

Platelets 320,000
/ μ L

Leukocyte
count 14,000
cells/ μ L

Neutrophils 50%

Eosinophils 28%

Lymphocytes 17%

count

cells/ μ L

Neutrophils 50%

Eosinophils 28%

Lymphocytes 17%

Monocytes 5%

Serum antibodies against neutrophil myeloperoxidase are positive. This patient most likely has which of the following conditions?

- ☐ A. Allergic bronchopulmonary aspergillosis
- ☐ B. Anti-glomerular basement membrane antibody disease
- ☐ C. Carpal tunnel syndrome
- ☐ D. Eosinophilic granulomatosis with polyangiitis
- ☐ E. Idiopathic pulmonary fibrosis
- ☐ F. Systemic sclerosis

Eosinophils 28%

Lymphocytes 17%

Monocytes 5%

Serum antibodies against **neutrophil myeloperoxidase** are positive. This patient most likely has which of the following conditions?

- ☐ A. ~~Allergic bronchopulmonary aspergillosis (2%)~~
- ☐ B. ~~Anti-glomerular basement membrane antibody disease (2%)~~
- ☐ C. ~~Carpal tunnel syndrome (10%)~~
- ☒ D. Eosinophilic granulomatosis with polyangiitis (77%)
- ☐ E. ~~Idiopathic pulmonary fibrosis (0%)~~
- ☐ F. Systemic sclerosis (6%)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Text Zoom



Settings

This patient most likely has **eosinophilic granulomatosis with polyangiitis** (Churg-Strauss). This small to medium vessel vasculitis is characterized by late-onset **asthma**, rhinosinusitis, and eosinophilia, though it can involve many other organ systems including the kidneys, gastrointestinal tract, and cardiovascular system. Asymmetric multifocal neuropathy (**mononeuritis multiplex**) is particularly common due to the **vasculitis** affecting the epineural vessels (eg, wrist drop due to radial nerve involvement). Other common manifestations include skin nodules, migratory/transient pulmonary infiltrates, and paranasal sinus abnormalities. In addition to peripheral **eosinophilia**, a frequent laboratory finding is antibodies against **neutrophil myeloperoxidase**, which most commonly have a pattern of perinuclear staining (p-ANCA).

(Choice A) Allergic bronchopulmonary aspergillosis (ABPA) can produce an asthma-like picture with eosinophilia and elevated IgE and IgG serum antibodies to *Aspergillus fumigatus*. However, systemic vasculitis and p-ANCA are not commonly associated with ABPA.

(Choice B) Pulmonary involvement in anti-glomerular basement membrane disease presents with cough, pulmonary infiltrates, and hemoptysis (not asthma-like symptoms). Patients have circulating autoantibodies against collagen IV, which damage alveolar and glomerular basement membranes.

(Choice C) Carpal tunnel syndrome is characterized by paresthesias and pain in the distribution of the



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Feedback



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End Block

pulmonary infiltrates, and hemoptysis (not asthma-like symptoms). Patients have circulating

autoantibodies against collagen IV, which damage alveolar and glomerular basement membranes.

(Choice C) Carpal tunnel syndrome is characterized by paresthesias and pain in the distribution of the median (not radial) nerve. Sensory symptoms are more prominent than motor symptoms during the initial presentation.

(Choice E) Idiopathic pulmonary fibrosis is a chronic fibrosing interstitial lung disease. There is no known association with p-ANCA, eosinophilia, or systemic vasculitis.

(Choice F) Pulmonary parenchymal involvement by systemic sclerosis (scleroderma) results in a chronic restrictive interstitial fibrosis. Antitopoisomerase I (Scl-70), anticentromere, and anti-RNA polymerase III antibodies are highly specific for systemic sclerosis.

Educational objective:

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) is a small to medium vessel vasculitis characterized by late-onset asthma, rhinosinusitis, and eosinophilia. Mononeuritis multiplex due to involvement of the epineural vessels of peripheral nerves is common.

References

- [Churg-Strauss syndrome: evolving concepts.](#)



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 30-year-old man is evaluated for 6 months of persistent pain in his right buttock and posterior thigh. He is a construction worker and has difficulty lifting heavy objects or climbing stairs. He has no history of back injury and no associated back pain. Past medical history is unremarkable. The patient does not use tobacco and drinks only moderate quantities of alcohol. On examination, the patient develops pain with forced adduction of the flexed thigh and internal rotation of the extended thigh against resistance. Further evaluation reveals possible entrapment of the sciatic nerve in the greater sciatic foramen. Which of the following structures passes through the foramen and occupies most of its volume?

- ☐ A. Coccygeus muscle
- ☐ B. Gluteus minimus muscle
- ☐ C. Obturator internus muscle
- ☒ D. Piriformis muscle
- ☐ E. Sacrospinous ligament
- ☐ F. Sacrotuberous ligament



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Feedback



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is a **construction** worker and has difficulty lifting heavy objects or climbing stairs. He has no history of back injury and no associated back pain. Past medical history is unremarkable. The patient does not use tobacco and drinks only moderate quantities of alcohol. On examination, the patient develops pain with forced **adduction** of the flexed thigh and internal rotation of the extended thigh against resistance. Further evaluation reveals possible **entrapment** of the **sciatic nerve** in the **greater sciatic foramen**. Which of the following structures passes through the foramen and occupies most of its volume?

- ☐ A. Coccygeus muscle (1%)
- ☐ B. Gluteus minimus muscle (7%)
- ☐ C. Obturator internus muscle (24%)
- ☒ D. Piriformis muscle (56%)
- ☐ E. Sacrospinous ligament (5%)
- ☐ F. Sacrotuberous ligament (4%)

Correct

56%



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10/16/2020

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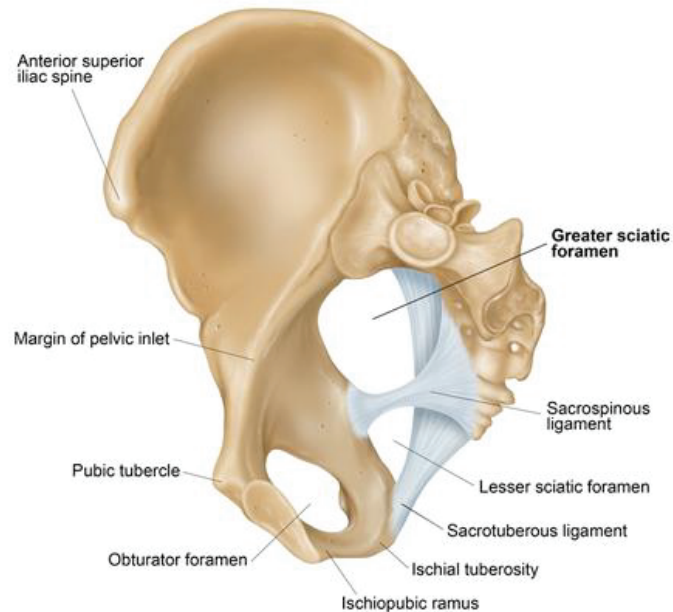
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Greater sciatic foramen



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Mark



Previous



Next



Full Screen



Tutorial



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Notes



Calculator



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The sciatic foramen is a pelvic opening serving as the major pathway for pelvic neurovascular structures to the lower limbs. It is divided into greater and lesser sciatic foramina by the sacrospinous ligament (**Choice E**). The **greater sciatic foramen** is bordered anterolaterally by the greater sciatic notch of the ilium, inferiorly by the ischial spine and sacrospinous ligament, superiorly by the anterior sacroiliac ligament, and posteromedially by the sacrotuberous ligament (**Choice F**).

The **piriformis** originates on the anterior aspect of the sacrum and occupies most of the space in the greater sciatic foramen. It inserts on the greater trochanter of the femur and acts to externally rotate the thigh when extended and abduct the thigh when flexed. Structures running above the piriformis include the superior gluteal vessels and superior gluteal nerve. Structures crossing below the piriformis include the inferior gluteal vessels, internal pudendal vessels, and multiple nerves (most notably the **sciatic** nerve). Muscle injury or hypertrophy can compress the sciatic nerve to cause sciatica-like symptoms (eg, pain, tingling, and numbness in the buttocks and along the nerve distribution) known as **piriformis syndrome**. The muscle can be tender with deep palpation or on stretching with adduction and internal rotation.

(Choice A) The coccygeus muscle is a pelvic floor muscle anterior to the sacrospinous ligament and combines with the levator ani to form the pelvic diaphragm.

(Choice B) The gluteus minimus is the smallest of the 3 gluteal muscles and is immediately beneath the



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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combines with the levator ani to form the pelvic diaphragm.

(Choice B) The gluteus minimus is the smallest of the 3 gluteal muscles and is immediately beneath the gluteus medius. It works with the gluteus medius to stabilize the hip and abduct the thigh when the limb is extended.

(Choice C) The obturator internus is a fan-shaped muscle originating from the medial surface of the obturator membrane, ischium, and pubic rim. It exits the pelvis through the lesser sciatic foramen and inserts on the greater trochanter of the femur, where it functions similarly to the piriformis.

Educational objective:

The piriformis passes through the greater sciatic foramen and is involved with external hip rotation. Muscle injury or hypertrophy can compress the sciatic nerve in the foramen, causing piriformis syndrome.

References

- [Piriformis syndrome: a cause of nondiscogenic sciatica.](#)

Anatomy

Rheumatology/Orthopedics & Sports

Sciatic neuropathy

Subject

System

Topic

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Previous



Next



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Tutorial



Lab Values



Notes



Calculator



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Text Zoom



Settings

A 22-year-old man comes to the office due to 3 months of progressive back pain. He has also had intermittent subjective fever. The patient emigrated from Nepal for a master's program 6 months ago. He has no other medical conditions, takes no medication, and does not use tobacco, alcohol, or illicit drugs. Temperature is 38.3 C (100.9 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. BMI is 19 kg/m². Tenderness is noted over the lumbar spine; flexion, extension, and rotation of the spine are limited due to pain and muscle spasm. MRI of the lower spine reveals partial destruction of the anterior portion of the L1-L3 vertebral bodies and a fluid collection beneath the anterior longitudinal ligament. Which of the following is the most likely diagnosis?

- ☐ A. Hodgkin lymphoma
- ☐ B. Osteosarcoma
- ☐ C. Rhabdomyosarcoma
- ☐ D. *Staphylococcus aureus* infection
- ☐ E. Tuberculosis



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Feedback



Suspend



End Block



intermittent subjective fever. The patient emigrated from Nepal for a master's program 6 months ago. He has no other medical conditions, takes no medication, and does not use tobacco, alcohol, or illicit drugs. Temperature is 38.3 C (100.9 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. BMI is 19 kg/m². Tenderness is noted over the lumbar spine; flexion, extension, and rotation of the spine are limited due to pain and muscle spasm. MRI of the lower spine reveals partial destruction of the anterior portion of the L1-L3 vertebral bodies and a fluid collection beneath the anterior longitudinal ligament. Which of the following is the most likely diagnosis?

- ☐ A. Hodgkin lymphoma (1%)
- ☐ B. Osteosarcoma (4%)
- ☐ C. Rhabdomyosarcoma (1%)
- ☐ D. *Staphylococcus aureus* infection (16%)
- ✓ ☒ E. Tuberculosis (76%)

Correct

76%

01 min, 01 sec

02/13/2021

Block Time Remaining: 00:34:16

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Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient who recently emigrated from a tuberculosis-endemic region (Nepal) now has progressive back pain, intermittent fever, and vertebral bone destruction with an adjacent fluid collection (abscess), raising strong suspicion for ***Mycobacterium tuberculosis spondylitis*** (Pott disease).

Primary tuberculosis infections are acquired via inhalation and cause localized pulmonary infection that is typically contained over weeks by the **cell-mediated immune response**. However, transient bacteremia can occur prior to containment and result in the **hematogenous seeding** of highly vascular organs (eg, spleen, liver, bones); the vertebrae are particularly likely to be affected due to their extensive venous plexuses.

Pott disease typically occurs months to years following primary pulmonary infection. It is characterized by intermittent fever and slowly worsening pain in the lumbar or lower thoracic spine. The infection frequently spreads behind the anterior ligament to the adjacent vertebrae and intervertebral disc space, leading to **contiguous bone destruction** and **abscess** formation.

(Choice A) Hodgkin lymphoma is often associated with intermittent fever but typically presents with regional adenopathy and/or a mediastinal mass. Vertebrae destruction and a fluid collection are not common features.

(Choices B and C) Osteosarcoma is the most common primary bone tumor in young adults; however, the long bones are primarily affected, and imaging typically shows a lytic bone lesion. Rhabdomyosarcoma is



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Feedback

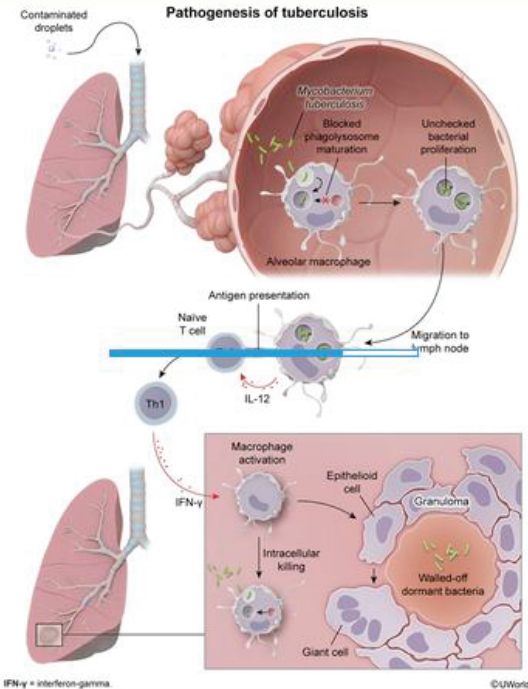


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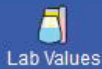
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Exhibit Display



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long bones are primarily affected, and imaging typically shows a lytic bone lesion. Rhabdomyosarcoma is



common features.

(Choices B and C) Osteosarcoma is the most common primary bone tumor in young adults; however, the long bones are primarily affected, and imaging typically shows a lytic bone lesion. Rhabdomyosarcoma is a soft-tissue sarcoma that usually arises in the head/neck, genitourinary tract, or extremities; imaging usually reveals a soft-tissue mass. Neither is typically associated with fever and a fluid collection; these features make an infectious process far more likely.

(Choice D) *Staphylococcus aureus* is the most common cause of spinal epidural abscess. Although the radiographic appearance can be similar to Pott disease, most cases arise in the setting of intravenous drug use, hematogenous spread of a distant infection (eg, endocarditis), or direct inoculation during a spinal procedure. This patient's recent emigration from a tuberculosis-endemic area makes Pott disease more likely.

Educational objective:

Mycobacterium tuberculosis spondylitis (Pott disease) is usually the result of hematogenous seeding of vertebrae from primary pulmonary infection. Manifestations typically arise months or years later (due to reactivation) and include chronic, progressive back pain, fever, and radiographic evidence of vertebral bone destruction and fluid collection.



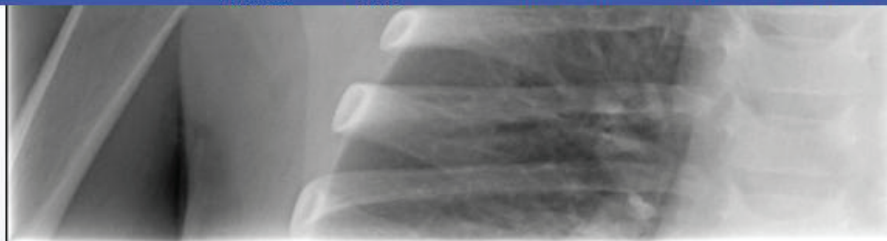
A 3-year-old boy is brought to the emergency department after falling off a jungle gym. The boy tried to catch himself and landed on his outstretched arms. He did not lose consciousness and has been crying inconsolably since he fell. Pulse is 140/min; all other vital signs are within normal limits. Physical examination reveals tenderness and swelling over the anterior portion of his right shoulder with crepitus over the swollen area. An x-ray of his right shoulder is shown below.



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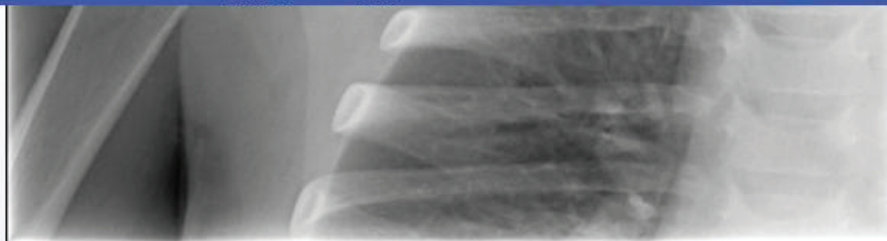
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Tension from which of the following muscles is most likely responsible for displacement of the distal bone fragment?

- ☐ A. Biceps
- ☐ B. Deltoid
- ☐ C. Levator scapulae
- ☐ D. Pectoralis minor
- ☐ E. Teres minor

Submit



Tension from which of the following muscles is most likely responsible for displacement of the distal bone fragment?

- ☐ A. Biceps (5%)
- ☒ B. Deltoid (37%)
- ☐ C. Levator scapulae (16%)
- ☐ D. Pectoralis minor (31%)
- ☐ E. Teres minor (8%)

Correct

37%



32 secs



01/29/2021

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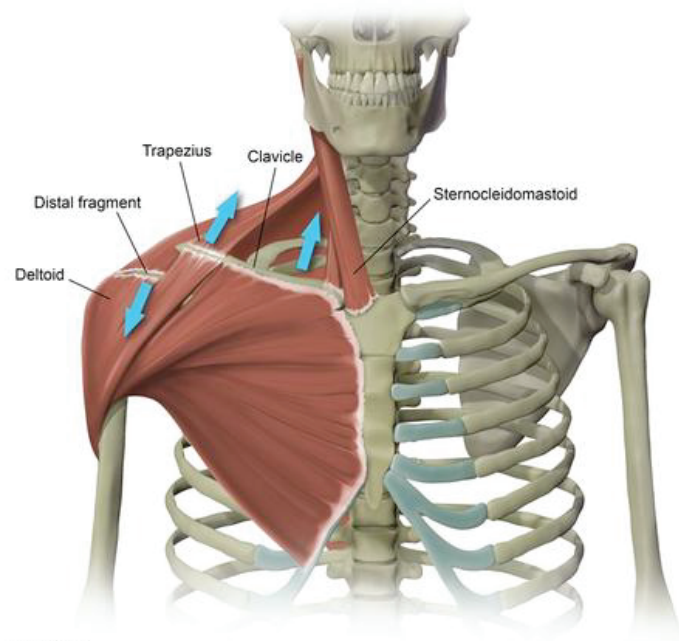
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Exhibit Display

Distal clavicle fracture



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This patient has a displaced **fracture** of the **distal clavicle**, a commonly fractured bone. The clavicle is the only bone affixing the upper extremity and shoulder girdle to the thorax, and it can be subjected to significant forces during an injury, such as a fall onto the shoulder or outstretched arm.

Because of their attachments on the clavicle, numerous muscles can apply tension on the proximal or distal bone fragments of a clavicle fracture. The anterior portion of the **deltoid muscle** originates on the distal clavicle and inserts onto the humerus. Normally, this part of the muscle acts to abduct, flex, and medially rotate the humerus. However, in a distal clavicle fracture, deltoid muscle tone and the weight of the upper extremity act to pull the **distal fragment** in the **inferolateral** direction. The proximal segment of the bone is pulled in the superomedial direction by the sternocleidomastoid and trapezius muscles. The net effect is to displace the fracture, which increases the risk of **nonunion**.

(Choice A) The biceps brachii originates on the supraglenoid tubercle (long head) and coracoid process (short head) of the scapula. It inserts onto the radial tuberosity and bicipital aponeurosis of the forearm.

(Choice C) The levator scapulae originates on the C1-C4 vertebrae and spans to the superomedial scapula. This muscle raises the scapula and rotates the acromion inferiorly.

(Choice D) The pectoralis minor spans from the coracoid process of the scapula to the third, fourth, and fifth ribs and stabilizes the scapula against the thoracic wall.

to displace the fracture, which increases the risk of nonunion.

(Choice A) The biceps brachii originates on the supraglenoid tubercle (long head) and coracoid process (short head) of the scapula. It inserts onto the radial tuberosity and bicipital aponeurosis of the forearm.

(Choice C) The levator scapulae originates on the C1-C4 vertebrae and spans to the superomedial scapula. This muscle raises the scapula and rotates the acromion inferiorly.

(Choice D) The pectoralis minor spans from the coracoid process of the scapula to the third, fourth, and fifth ribs and stabilizes the scapula against the thoracic wall.

(Choice E) The teres minor spans from the lateral scapula to the greater tubercle of the humerus. It stabilizes the glenohumeral joint and laterally rotates the humerus.

Educational objective:

The clavicle is commonly fractured in children after a fall on an outstretched arm. In a distal clavicle fracture, the deltoid muscle and the weight of the arm cause inferolateral displacement of the distal fragment, whereas the sternocleidomastoid and trapezius muscles cause superomedial displacement of the proximal fragment.

References

- [Clavicle fractures: a review of the literature and update on treatment.](#)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 34-year-old man is evaluated in the emergency department due to difficulty walking. He was installing new shingles on his roof when he fell to the ground and sustained a puncture injury to his right leg. On physical examination, the right foot is dorsiflexed and everted. The patient is unable to stand on his tiptoes. Muscular strength at the knee and hip appear intact. Pedal and tibial pulses are +2 and symmetric. X-rays of his right leg are negative for fracture. This patient is most likely to have sensory loss over which of the following areas?

- ☐ A. Anterior thigh
- ☐ B. Dorsal foot
- ☐ C. Medial foot
- ☐ D. Medial leg
- ☐ E. Plantar foot

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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



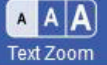
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 34-year-old man is evaluated in the emergency department due to difficulty walking. He was installing new shingles on his roof when he fell to the ground and sustained a puncture injury to his right leg. On physical examination, the right foot is dorsiflexed and everted. The patient is unable to stand on his tiptoes. Muscular strength at the knee and hip appear intact. Pedal and tibial pulses are +2 and symmetric. X-rays of his right leg are negative for fracture. This patient is most likely to have sensory loss over which of the following areas?

- ☐ A. Anterior thigh (1%)
- ☐ B. Dorsal foot (16%)
- ☐ C. Medial foot (9%)
- ☐ D. Medial leg (9%)
- ☒ E. Plantar foot (62%)

Correct

 62%
Answered correctly 01 min, 08 secs
Time Spent 02/04/2021
Last Updated

Block Time Remaining: 00:35:56

TUTOR

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Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



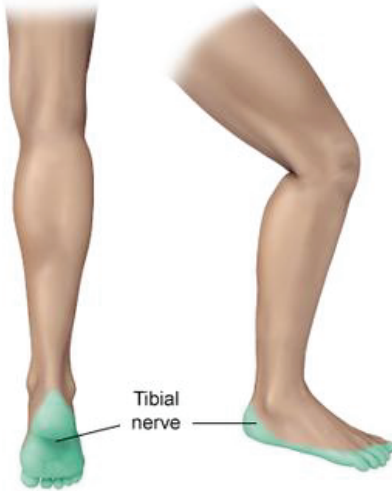
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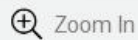
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Exhibit Display

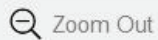
Tibial nerve

| Nerve | Motor function | Cutaneous innervation |
|--------------|---|---|
| Tibial nerve | Foot plantar flexion & inversion, toe flexion |  |

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New



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0



Feedback



Suspend



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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The **tibial nerve** is the large medial branch of the sciatic nerve and descends through the popliteal fossa together with the popliteal vein and artery. It then traverses the posterior compartment of the leg deep to the soleus muscle. After providing motor innervation to the posterior compartment muscles, the nerve enters the plantar aspect of the foot through the tarsal tunnel (between the flexor retinaculum and medial surfaces of the talus and calcaneus). Here, it divides into the medial and lateral plantar nerves, providing **sensory** innervation over the **sole** of the foot and motor innervation to the intrinsic foot muscles.

Injury to the nerve at the popliteal fossa (eg, deep penetrating trauma, knee surgery) can cause weakness on **foot plantarflexion** because the nerve innervates the gastrocnemius, soleus, and plantaris muscles. Weakness may also be evident on foot **inversion** (eg, tibialis posterior muscle) and **toe flexion** (eg, flexor digitorum longus and flexor hallucis longus muscles). Consequently, patients often present with the foot held in a calcaneovalgus position (eg, dorsiflexed and everted). In contrast, injury to the tibial nerve at the tarsal tunnel may cause sensory loss over the sole with intrinsic foot muscle weakness. However, plantarflexion and inversion remain intact as fibers innervating these muscles branch off more proximally.

(Choice A) The cutaneous branches of the **femoral nerve** innervate most of the skin over the anterior thigh.

(Choice B) The **superficial peroneal nerve** innervates the lateral leg and dorsum of the foot except for the



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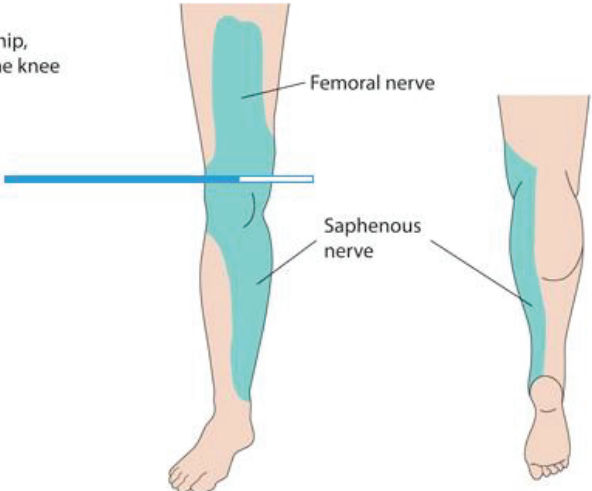
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Exhibit Display

Important nerves in the leg

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---------------|--|--|
| Femoral nerve | Leg flexion at the hip, leg extension at the knee |  |

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(Choice B) The saphenous nerve innervates the lateral leg and dorsum of the foot except for the

Block Time Remaining: 00:35:56

TUTOR

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End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice A) The cutaneous branches of the **femoral nerve** innervate most of the skin over the anterior thigh.

(Choice B) The **superficial peroneal nerve** innervates the lateral leg and dorsum of the foot, except for the skin between the great toe and second toe, which is innervated by the **deep peroneal nerve**.

(Choice C) The medial aspect of the foot is innervated by the superficial peroneal nerve, a branch of the common peroneal nerve, and by the saphenous nerve.

(Choice D) Cutaneous branches of the saphenous nerve innervate the skin of the medial leg. The saphenous nerve is a branch of the femoral nerve and courses to the medial leg together with the great saphenous vein.

Educational objective:

The tibial nerve may be injured at the level of the popliteal fossa due to deep penetrating trauma or knee surgery. Patients typically have weakness on foot plantarflexion, foot inversion, and toe flexion, with sensory loss over the sole.

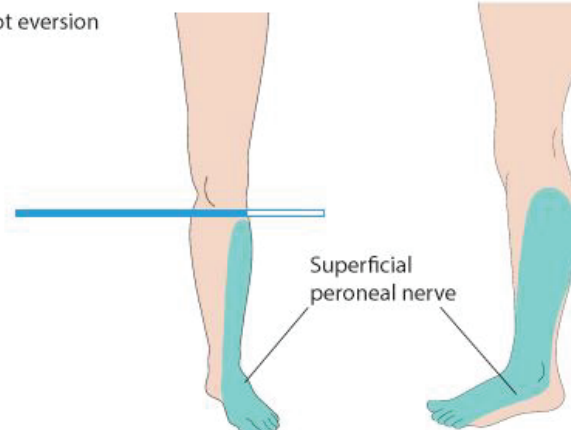
References

- **Entrapment neuropathies of the lower extremity.**
- **Lower extremity nerve trauma**



(Choice A) The cutaneous branches of the femoral nerve innervate most of the skin over the anterior

Exhibit Display

| Nerve | Motor function | Cutaneous innervation |
|----------------------------|----------------|--|
| Superficial peroneal nerve | Foot eversion |  |

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Zoom Out

Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

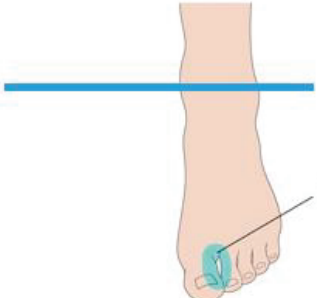
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Settings

(Choice A) The cutaneous branches of the femoral nerve innervate most of the skin over the anterior

Exhibit Display

Important nerves in the leg

| Nerve | Motor function | Region of sensory loss with neuropathy |
|---------------------|----------------------------------|--|
| Deep peroneal nerve | Foot dorsiflexion, toe extension |  |

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Zoom Out

Reset

New | Existing

My Notebook





A 14-year-old boy comes to the office with his mother due to progressive anterior knee pain affecting the left leg for the past 2 months. The pain started as a mild ache toward the end of a hiking trip. The patient reports no fever, night sweats, or trauma to the knee. On physical examination, he has a normal gait. The hips, knees, and ankles have full range of motion. An area of mild swelling tender to palpation is located about 3 cm below the inferior border of the patella. An x-ray of the left knee is shown in the [exhibit](#). Overuse of which of the following muscles most likely contributed to this patient's condition?

- ☐ A. Biceps femoris
- ☐ B. Popliteus
- ☐ C. Quadriceps femoris
- ☐ D. Sartorius
- ☐ E. Tibialis anterior

Submit



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

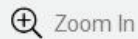


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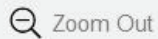


Settings

Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook



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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color


Text Zoom

Settings

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- ☐ A. Biceps femoris (5%)
- ☐ B. Popliteus (3%)
- ☒ C. Quadriceps femoris (69%)
- ☐ D. Sartorius (2%)
- ☐ E. Tibialis anterior (18%)

Correct

 69%
Answered correctly 17 secs
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Last Updated

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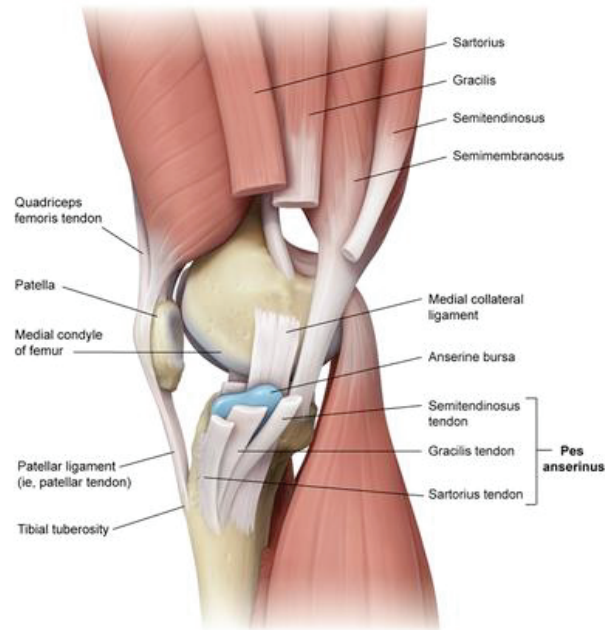
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Exhibit Display

Medial knee & pes anserinus



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New | Existing

My Notebook

This patient has **Osgood-Schlatter disease** (OSD), a common cause of knee pain in adolescents due to overuse of the **quadriceps** muscle group (ie, rectus femoris, vastus intermedius, vastus lateralis, vastus medialis). The quadriceps is located in the anterior thigh and is responsible for **knee extension**. Its tendon initially inserts at the superior pole of the patella. The tendon envelops the patella and continues as the patellar ligament, which then inserts at the **tibial tubercle**. As a result, contraction of the quadriceps (eg, hiking, running) creates traction on the tibial tubercle.

In skeletally immature children, the tibial tubercle forms as a **secondary ossification center** (apophysis) of the tibia, and the cartilaginous nature of the developing tibial tuberosity makes it more prone to injury compared to fully ossified bone in adults. Repetitive quadriceps contraction results in chronic **avulsion/fragmentation of the tubercle**, with corresponding tenderness and swelling, as seen in this patient.

(Choice A) The biceps femoris, along with the semitendinosus and semimembranosus, forms the **hamstring muscle group** in the posterior thigh; it is responsible for hip extension and knee flexion. The long head of the biceps femoris originates from the ischial tuberosity, whereas the short head originates from the inferior third of the linea aspera. Both insert at the head of the fibula.

(Choice B) The popliteus originates from the lateral condyle of the femur and lateral meniscus and inserts at the proximal shaft of the tibia. It flexes and medially rotates the leg (unlocks an extended knee).

Exhibit Display

Osgood-Schlatter disease



Elevated and
fragmented tibial
tubercle

Zoom In

Zoom Out

Reset

New | Existing

My Notebook

at the proximal shaft of the tibia. It flexes and medially rotates the leg (unlocks an extended knee).

Block Time Remaining: 00:36:13

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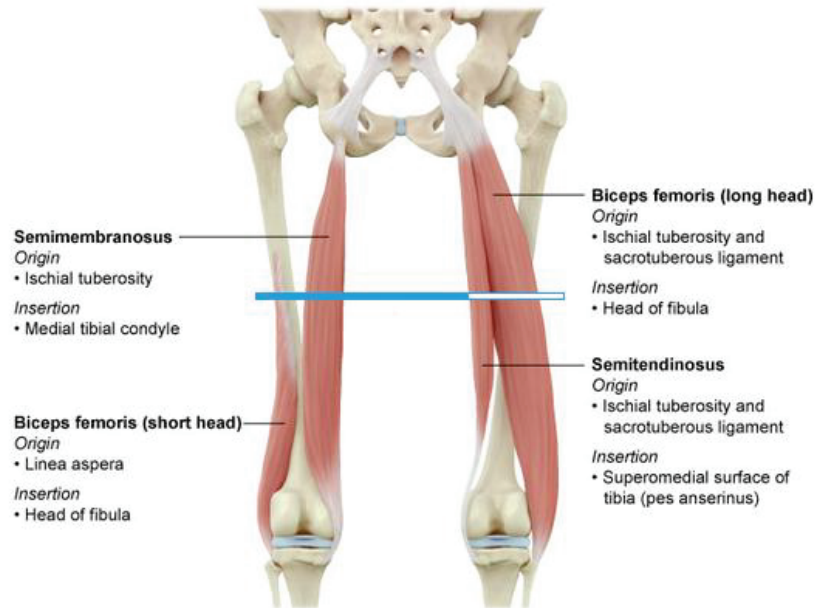
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Exhibit Display

Major hip extensors and knee flexors



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at the proximal shaft of the tibia. It flexes and medially rotates the leg (unlocks an extended knee).

Block Time Remaining: 00:36:13

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Feedback

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(Choice B) The popliteus originates from the lateral condyle of the femur and lateral meniscus and inserts at the proximal shaft of the tibia. It flexes and medially rotates the leg (unlocks an extended knee).

(Choice D) The **sartorius** originates from the anterior superior iliac spine and inserts at the superomedial surface of the tibia. Because of its oblique orientation across the anterior thigh, the sartorius is responsible for hip flexion, external rotation, and abduction, as well as knee flexion. This combination of movements is needed to sit in a cross-legged position.

(Choice E) The **tibialis anterior** originates from the lateral condyle of the tibia, the upper half of the lateral tibia, and the interosseus membrane. It inserts at the cuneiform and first metatarsal. It is responsible for ankle dorsiflexion and foot inversion.

Educational objective:

Repetitive traction at the tibial tubercle due to quadriceps contraction can lead to avulsion and fragmentation of the tibial tubercle in skeletally immature children, causing Osgood-Schlatter disease.

References





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

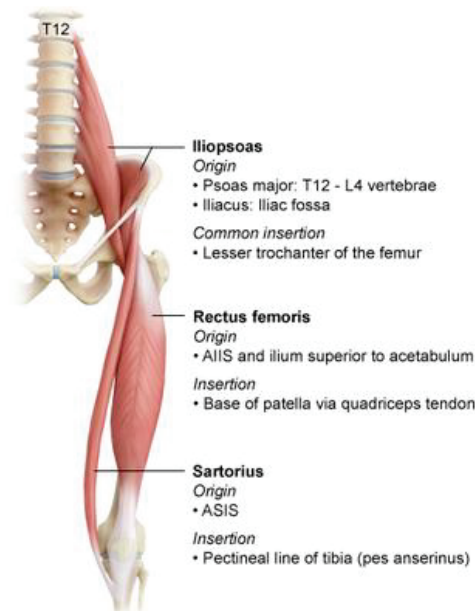
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Exhibit Display

Muscular attachments of the major hip flexors

**Iliopsoas***Origin*

- Psoas major: T12 - L4 vertebrae
- Iliacus: Iliac fossa

Common insertion

- Lesser trochanter of the femur

Rectus femoris*Origin*

- AIIS and ilium superior to acetabulum

Insertion

- Base of patella via quadriceps tendon

Sartorius*Origin*

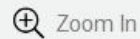
- ASIS

Insertion

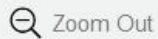
- Pectineal line of tibia (pes anserinus)

*AIIS = anterior inferior iliac spine; ASIS = anterior superior iliac spine

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Zoom In



Zoom Out



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References

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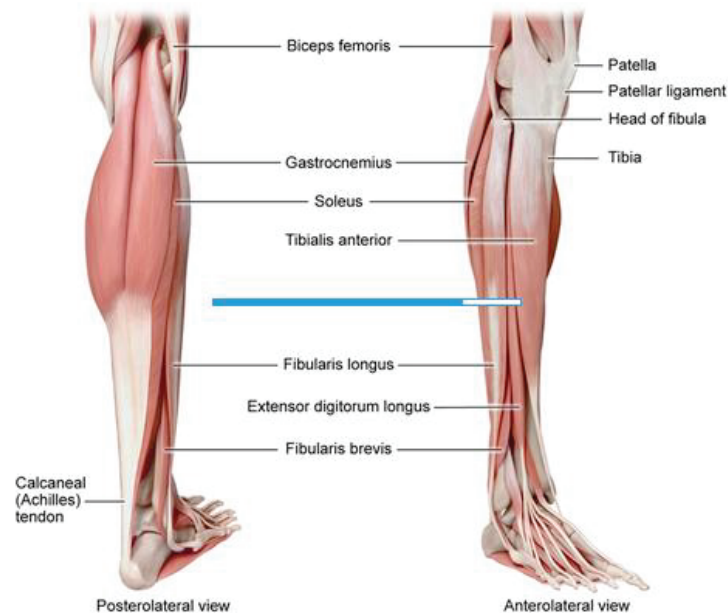


End Block

hamstring muscle group in the posterior thigh; it is responsible for hip extension and knee flexion. The long

Exhibit Display

Muscles of the leg



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Zoom Out

Reset

New | Existing

My Notebook

References

Block Time Remaining: 00:36:13

TUTOR

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Suspend

End Block

A 56-year-old man comes to the emergency department due to persistent left wrist pain. While walking his dog 5 hours ago, he fell forward onto the ground and landed on his outstretched hand. Examination shows mild left wrist swelling with preserved range of motion. There is point tenderness over the dorsolateral aspect of the wrist between the tendons of the extensor pollicis longus and extensor pollicis brevis. An x-ray of the left wrist is shown in the image below:





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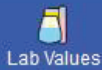
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Full Screen



Tutorial



Lab Values



Notes



Calculator



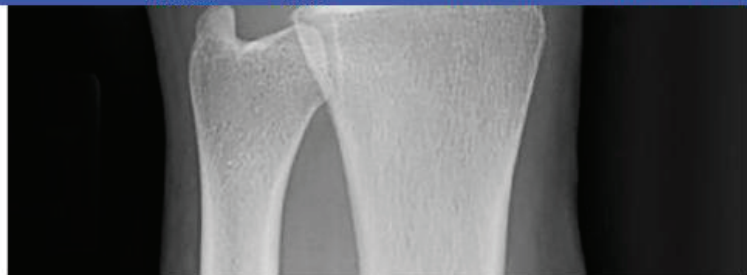
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Text Zoom



Settings



This patient is at greatest risk for developing which of the following complications?

- ☐ A. Avascular necrosis
- ☒ B. Carpal tunnel syndrome
- ☐ C. Compartment syndrome
- ☐ D. Dupuytren contracture
- ☐ E. Guyon canal syndrome

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Mark



Previous



Next



Full Screen



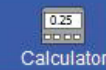
Tutorial



Lab Values



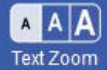
Notes



Calculator



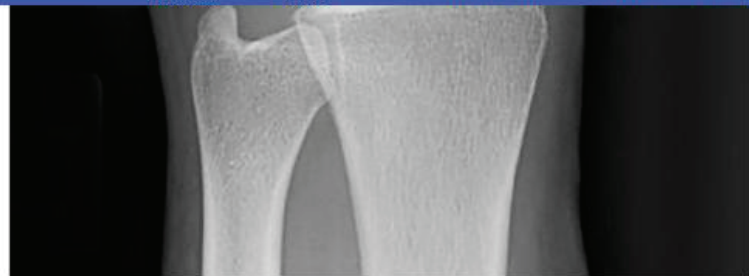
Reverse Color



Text Zoom



Settings



This patient is at greatest risk for developing which of the following complications?

- ☒ A. Avascular necrosis (77%)
- ☐ B. Carpal tunnel syndrome (7%)
- ☐ C. Compartment syndrome (2%)
- ☐ D. Dupuytren contracture (2%)
- ☐ E. Guyon canal syndrome (9%)

Correct

77%



14 secs



02/09/2021

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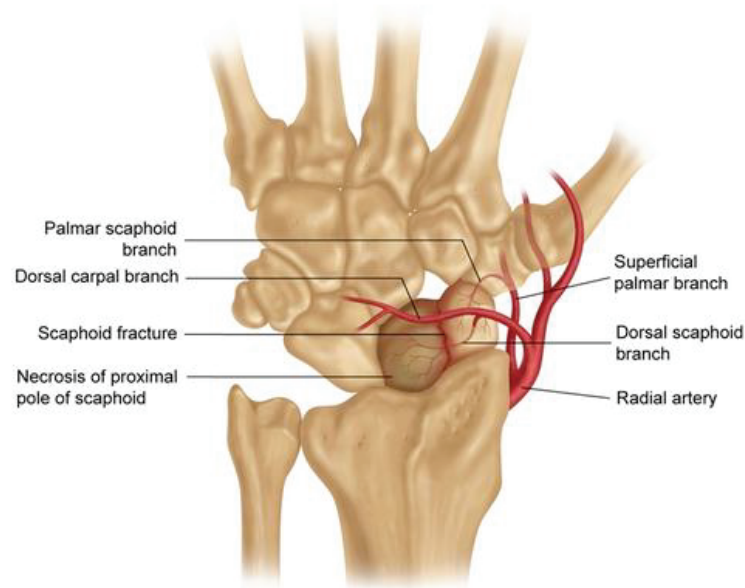
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Scaphoid avascular necrosis



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Scaphoid fractures are the most common carpal bone fracture and frequently result from a **fall** on an **outstretched hand** that causes direct axial compression or hyperextension of the wrist. A scaphoid fracture should be suspected in any patient with persistent wrist pain and **tenderness** in the **anatomic snuffbox**—a shallow, triangular depression at the dorsoradial wrist defined by the following borders:

- Medial: tendon of the extensor pollicis longus
- Lateral: tendons of the abductor pollicis longus and extensor pollicis brevis
- Proximal: styloid process of the radius
- **Floor: scaphoid** and trapezium bones

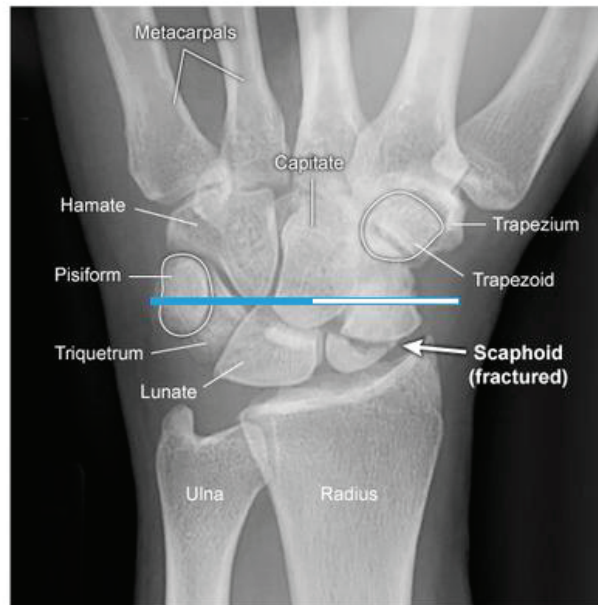
The main blood supply to the scaphoid is provided by the dorsal scaphoid branch of the radial artery; this branch enters near the bone's distal pole and then proceeds in a retrograde manner to provide blood supply to the proximal pole. Because fracture of the scaphoid can easily interrupt this retrograde flow, the fractured scaphoid is at risk for **avascular necrosis** of the proximal pole and fracture **nonunion**.

(Choice B) Carpal tunnel syndrome is caused by median nerve compression at the wrist within the **carpal tunnel**. It is mostly commonly nontraumatic in origin, but when it does occur following trauma (eg, fall on an outstretched hand), it is typically due to palmar dislocation of the lunate into the carpal tunnel space.

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Scaphoid fracture



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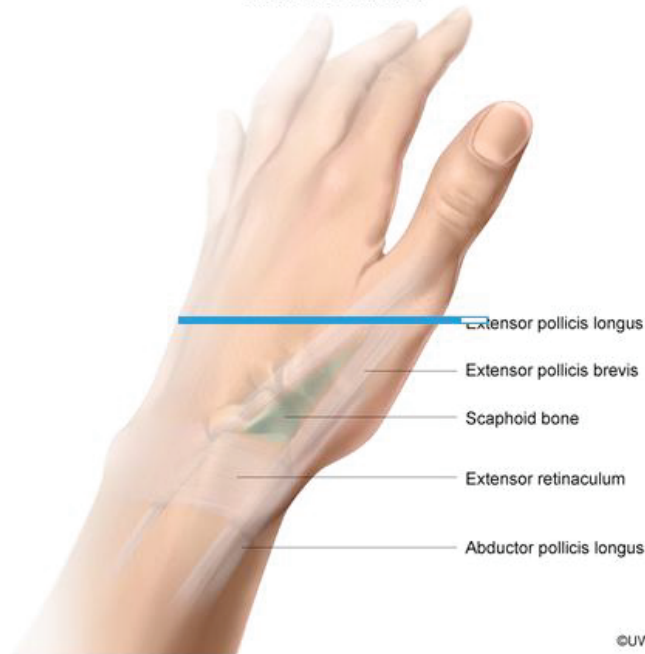
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Anatomic snuffbox



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Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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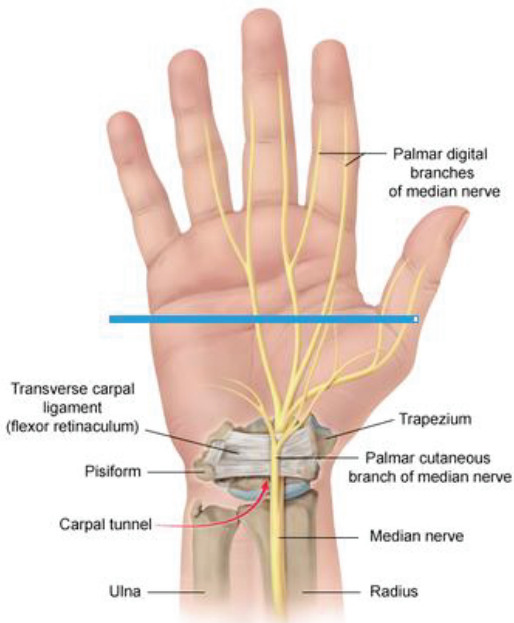


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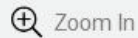
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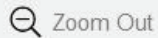
Carpal tunnel, palmar view



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Reset



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Existing



My Notebook

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0



Feedback



Suspend



End Block



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) Carpal tunnel syndrome is caused by median nerve compression at the wrist within the **carpal tunnel**. It is mostly commonly nontraumatic in origin, but when it does occur following trauma (eg, fall on an outstretched hand), it is typically due to palmar dislocation of the lunate into the carpal tunnel space.

(Choice C) Acute compartment syndrome occurs when increased pressure within a fascial compartment (eg, intracompartmental bleeding, muscle swelling) compromises blood circulation within that space. It typically develops after significant trauma, particularly long bone fractures of the leg or forearm.

(Choice D) **Dupuytren contracture** is a slowly progressive fibroproliferative disease of the palmar fascia. Nodules form on the fascia, eventually resulting in contractures that draw the fingers into flexion.

(Choice E) Guyon canal syndrome is caused by compression of the ulnar nerve at the wrist within **Guyon canal**. It can develop following a fall on an outstretched hand but typically occurs due to fracture of the hook of the hamate, which forms the lateral bony wall of Guyon canal.

Educational objective:

Fracture of the scaphoid bone may result from a fall on an outstretched hand and should be suspected if examination shows tenderness in the anatomic snuff box. Scaphoid fracture can disrupt retrograde blood supply to the proximal scaphoid, increasing risk of avascular necrosis.

References





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

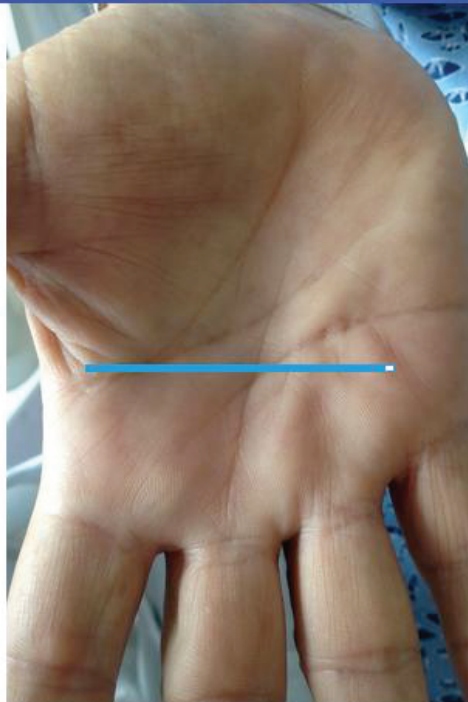
Calculator

Reverse Color

Text Zoom

Settings

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Zoom Out

Reset

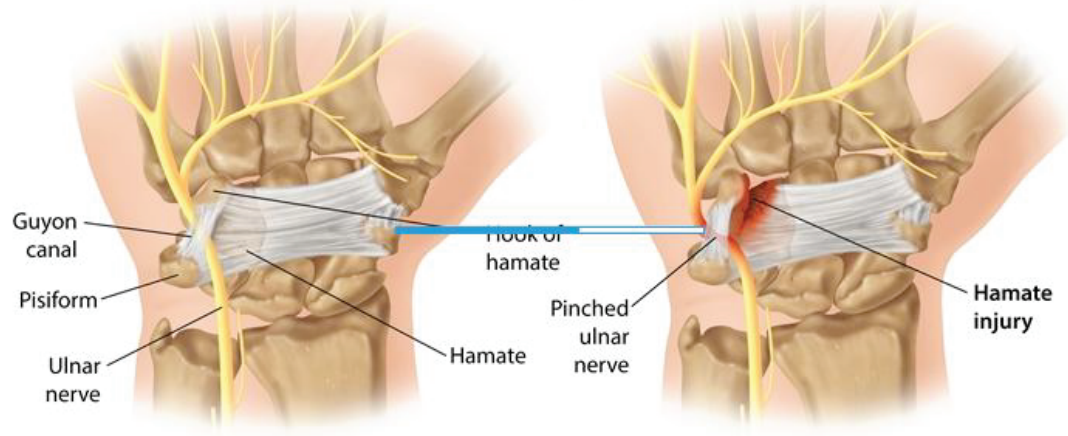
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Exhibit Display

Guyon canal syndrome
"ulnar trap"



Normal

Guyon syndrome

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A 65-year-old man comes to the emergency department with a 3-day history of headaches localized to the right temporal region. The headaches are accompanied by intermittent blurring of vision in both eyes. He has also felt fatigued for the past week, with stiffness in his shoulders and hips. On examination, temperature is 37.5 C (99.5 F). There is tenderness on palpation of the right temporal region with enlargement of the underlying artery, as shown in the [exhibit](#). Fundusoscopic examination reveals edematous optic discs in both eyes. The patient has limited active abduction of the shoulder joints bilaterally. Laboratory studies show an erythrocyte sedimentation rate of 115 mm/hr. Which of the following is the most important mediator of this patient's current condition?

- ☐ A. Antibodies to myeloperoxidase
- ☐ B. Antibodies to proteinase-3
- ☐ C. B cell-activating factor
- ☐ D. Interleukin-6
- ☐ E. Matrix metalloproteinase





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

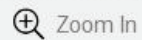


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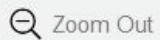


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Zoom Out



Reset



New



Existing



My Notebook



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Feedback



Suspend



End Block



right temporal region. The headaches are accompanied by intermittent blurring of vision in both eyes. He has also felt fatigued for the past week, with stiffness in his shoulders and hips. On examination, temperature is 37.5 C (99.5 F). There is tenderness on palpation of the right temporal region with enlargement of the underlying artery, as shown in the [exhibit](#). Funduscopic examination reveals **edematous optic discs** in both eyes. The patient has limited active abduction of the shoulder joints bilaterally. Laboratory studies show an erythrocyte sedimentation rate of 115 mm/hr. Which of the following is the most important mediator of this patient's current condition?

- ☐ A. Antibodies to myeloperoxidase (12%)
- ☐ B. Antibodies to proteinase-3 (12%)
- ☐ C. B cell-activating factor (5%)
- ☒ D. Interleukin-6 (54%)
- ☐ E. Matrix metalloproteinase (16%)

Correct



54%

Answered correctly



01 min, 15 secs

Time spent



11/02/2020

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Feedback

Suspend

End Block

Explanation





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient with headaches, visual and muscular symptoms, an enlarged temporal artery, and elevated erythrocyte sedimentation rate has typical features of **giant cell arteritis** ([GCA] temporal arteritis) with associated polymyalgia rheumatica. GCA is the most common systemic vasculitis in persons of Northern European descent and occurs almost exclusively in patients age >50.

Although both humoral and cellular immune mechanisms have been implicated in the pathogenesis of GCA, cell-mediated processes are of primary importance. The **inflammatory infiltrate** in affected vessels is composed of lymphocytes (predominantly CD4-positive T cells) and macrophages and frequently contains multinucleated giant cells. The production of cytokines, in particular **interleukin-6** (IL-6), appears to closely correlate with the severity of the disease; a monoclonal antibody against IL-6 (tocilizumab) is effective in treating GCA.

(Choices A and B) Antibodies to myeloperoxidase and proteinase-3 are involved in the pathogenesis of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides such as microscopic polyangiitis and granulomatosis with polyangiitis.

(Choice C) B cell-activating factor (BAFF) is a cytokine belonging to the tumor necrosis factor ligand family. Inadequate levels of BAFF will lead to immunodeficiency, whereas excess levels can cause autoimmune diseases (eg, systemic lupus erythematosus).



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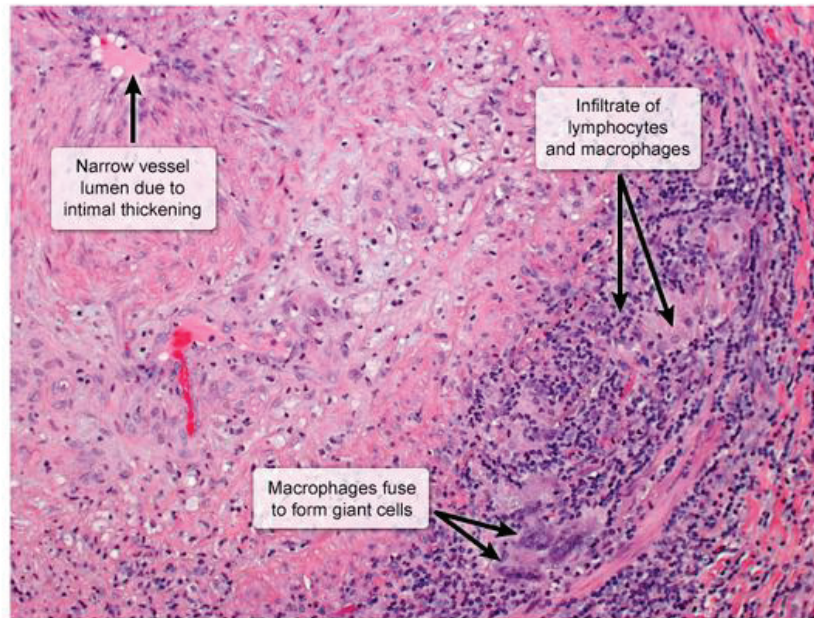
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Exhibit Display

Giant cell arteritis (temporal arteritis)



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Reset

New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides such as microscopic polyangiitis and granulomatosis with polyangiitis.

(Choice C) B cell-activating factor (BAFF) is a cytokine belonging to the tumor necrosis factor ligand family. Inadequate levels of BAFF will lead to immunodeficiency, whereas excess levels can cause autoimmune diseases (eg, systemic lupus erythematosus).

(Choice E) Matrix metalloproteinases are enzymes capable of degrading various extracellular matrix proteins and processing a number of bioactive molecules. They may be involved in cytokine inactivation but do not play a direct role in the pathogenesis of GCA.

Educational objective:

Cell-mediated immunity is the primary mechanism underlying giant cell arteritis. The production of cytokines, in particular interleukin-6, is an important driver of this process and closely correlates with the severity of symptoms.

References

- Pathogenesis of giant cell arteritis: new insight into the implication of CD161+ T cells.
- Pathogenesis of giant cell arteritis: more than just an inflammatory condition?





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 20-year-old college football quarterback is evaluated in the emergency department for acute right shoulder pain. One hour ago, the patient sustained a blow to the arm when tackled mid-throw during a championship game. On physical examination, there is flattening of the right deltoid muscle and insensitivity of the overlying skin to pinprick. Peripheral pulses in the upper extremities are intact. Which of the following injuries is most likely responsible for this patient's findings?

- ☐ A. Acromioclavicular joint subluxation
- ☐ B. Anterior dislocation of the humerus
- ☐ C. Clavicular fracture
- ☐ D. Fracture of the coracoid process
- ☐ E. Rotator cuff tear
- ☐ F. Spiral fracture of the midshaft humerus

Submit

Block Time Remaining: 00:37:44

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End Block

A 20-year-old college football quarterback is evaluated in the emergency department for **acute right shoulder pain**. One hour ago, the patient sustained a blow to the arm when tackled mid-throw during a championship game. On physical examination, there is **flattening** of the **right deltoid** muscle and insensitivity of the overlying skin to **pinprick**. Peripheral pulses in the upper extremities are intact. Which of the following injuries is most likely responsible for this patient's findings?

- ☐ A. Acromioclavicular joint subluxation (10%)
- ☒ B. Anterior dislocation of the humerus (71%)
- ☐ C. Clavicular fracture (4%)
- ☐ D. Fracture of the coracoid process (4%)
- ☐ E. Rotator cuff tear (5%)
- ☐ F. ~~Spiral fracture of the midshaft humerus (3%)~~

Correct

 71%
Answered correctly 01 min, 10 secs
Time Spent 11/26/2020
Last Updated



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

The glenohumeral joint is the most commonly dislocated joint in the body due to the shallow articulation between the humeral head and the glenoid fossa of the scapula. The shoulder may dislocate anteriorly, inferiorly, or posteriorly, but anterior dislocations are by far the most common. **Anterior dislocations** of the humerus classically follow a blow to an **externally rotated** and **abducted arm** (eg, throwing a football).

When the head of the humerus is displaced anteriorly, there is **flattening of the deltoid** prominence, protrusion of the acromion, and anterior axillary fullness (due to the humeral head's movement into this location). The **axillary nerve** is the nerve most commonly injured by anterior shoulder dislocations. It innervates the **deltoid and teres minor** muscles and provides sensory innervation to the skin overlying the **lateral shoulder**.

(Choice A) Acromioclavicular joint subluxation typically results from a downward blow on the tip of the shoulder and produces swelling and upward displacement of the clavicle. It is not usually associated with specific nerve injuries/deficits.

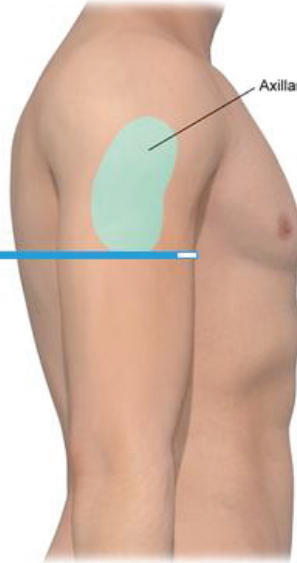
(Choice C) Clavicular fractures usually occur following direct trauma to the clavicle. Most fractures are in the middle third of the clavicle and produce local swelling and tenderness. Associated neurovascular damage is rare.

(Choice D) Fracture of the coracoid process of the scapula is rare. Individuals who engage in shotgun- or



Exhibit Display

Important nerves in the arm

| Motor function | Region of sensory loss with neuropathy |
|----------------|---|
| |  |

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(Choice D) Fracture of the coracoid process of the scapula is rare. Individuals who engage in shoulder- or

Block Time Remaining: 00:38:52

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Feedback

Suspend

End Block



the middle third of the clavicle and produce local swelling and tenderness. Associated neurovascular damage is rare.

(Choice D) Fracture of the coracoid process of the scapula is rare. Individuals who engage in shotgun- or rifle-related activities are most commonly affected.

(Choice E) Rotator cuff tears may occur during shoulder dislocation but do not cause nerve injury. The rotator cuff is made up of the subscapularis, supraspinatus, infraspinatus, and teres minor muscles/tendons.

(Choice F) A spiral fracture of the midshaft humerus may result from torsion produced during a fall on an outstretched hand. Patients present with swelling, bone crepitus, and ecchymoses of the arm. The radial nerve is commonly injured.

Educational objective:

Flattening of the deltoid muscle with acromial prominence after a shoulder injury suggests an anterior humerus dislocation. This injury most commonly results from a blow to an externally rotated and abducted arm. There is often associated axillary nerve injury, resulting in deltoid paralysis and loss of sensation over the lateral shoulder.

References





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 24-year-old African American woman comes to the office reporting left hip and pelvic pain. She has a constant, dull, achy pain at rest that is exacerbated by movement of the hip or weight bearing. Her medical history is significant for sickle cell disease, pneumococcal pneumonia, and acute chest syndrome. Temperature is 36.8 C (98.2 F), blood pressure is 110/65 mm Hg, pulse is 95/min, and respirations are 15/min. The patient appears calm but mildly uncomfortable. Cardiopulmonary examination is normal. Pedal pulses are full, and there is normal capillary refill and sensation in the feet. No redness or warmth is present over the hip joint, but she has decreased passive rotation, extension, and abduction at the hip. Which of the following is the most likely cause of this patient's pain?

- ☐ A. Acute bursitis
- ☐ B. Avascular necrosis
- ☐ C. Osteoarthritis
- ☐ D. Rheumatoid arthritis
- ☐ E. Septic arthritis



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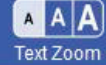
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constant, dull, achy pain at rest that is exacerbated by movement of the hip or weight bearing. Her medical history is significant for sickle cell disease, pneumococcal pneumonia, and acute chest syndrome. Temperature is 36.8 C (98.2 F), blood pressure is 110/65 mm Hg, pulse is 95/min, and respirations are 15/min. The patient appears calm but mildly uncomfortable. Cardiopulmonary examination is normal. Pedal pulses are full, and there is normal capillary refill and sensation in the feet. No redness or warmth is present over the hip joint, but she has decreased passive rotation, extension, and abduction at the hip. Which of the following is the most likely cause of this patient's pain?

- ☐ A. Acute bursitis (5%)
- ☒ B. Avascular necrosis (82%)
- ☐ C. Osteoarthritis (5%)
- ☐ D. Rheumatoid arthritis (1%)
- ☐ E. Septic arthritis (5%)

Correct

82%
Answered correctly01 min, 43 secs
Time spent11/15/2020
Last updated

Block Time Remaining: 00:40:35

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Osteonecrosis (avascular necrosis)

| | |
|--------------------------------|---|
| Causes | <ul style="list-style-type: none">• Thrombotic/embolicocclusion (eg, sickle cell, decompression sickness)• Glucocorticoids• Vascular inflammation/injury (vasculitis, radiation)• Excessive alcohol use• Traumatic fracture |
| Clinical manifestations | <ul style="list-style-type: none">• Pain on weight bearing• Decreased range of motion |
| Gross inspection | <ul style="list-style-type: none">• Wedge-shaped or geographic zone of necrosis• Articular cartilage is viable but may be distorted or detached from underlying bone |
| Microscopic inspection | <ul style="list-style-type: none">• Dead bony trabeculae with empty lacunae• Necrosis of surrounding adipocytes |

This patient, with hip pain, decreased range of motion, and underlying sickle cell disease, has

osteonecrosis (avascular necrosis) of the femoral head. Osteonecrosis occurs due to impaired blood



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

inspection

• Necrosis of surrounding adipocytes

This patient, with hip pain, decreased range of motion, and underlying sickle cell disease, has **osteonecrosis** (avascular necrosis) of the femoral head. Osteonecrosis occurs due to impaired blood supply to a segment of bone. The femoral head is the most common location, although other bones may be affected. Conditions associated with osteonecrosis include the following:

1. **Sickle cell disease** leads to thrombotic occlusion of arteries. Embolic occlusion (fat emboli, decompression sickness) can also cause osteonecrosis.
2. Injury to the vessel wall (**vasculitis**) causes impaired blood supply (eg, systemic lupus erythematosus).
3. High-dose **corticosteroid therapy** and **alcoholism** are also associated with osteonecrosis of the femoral head, although the mechanism is unknown.

Osteonecrosis of the femoral head presents with chronic, progressive groin and hip pain that is exacerbated by weight bearing. Physical examination reveals restricted movement in the affected joint, with no swelling, erythema, or warmth in the surrounding area. **Microscopic analysis** of the wedge-shaped zone of affected bone is notable for dead bony trabeculae (empty lacunae) and fat necrosis.

(Choice A) Trochanteric bursitis causes sharp, intermittent pain at the lateral hip and thigh. Pain is

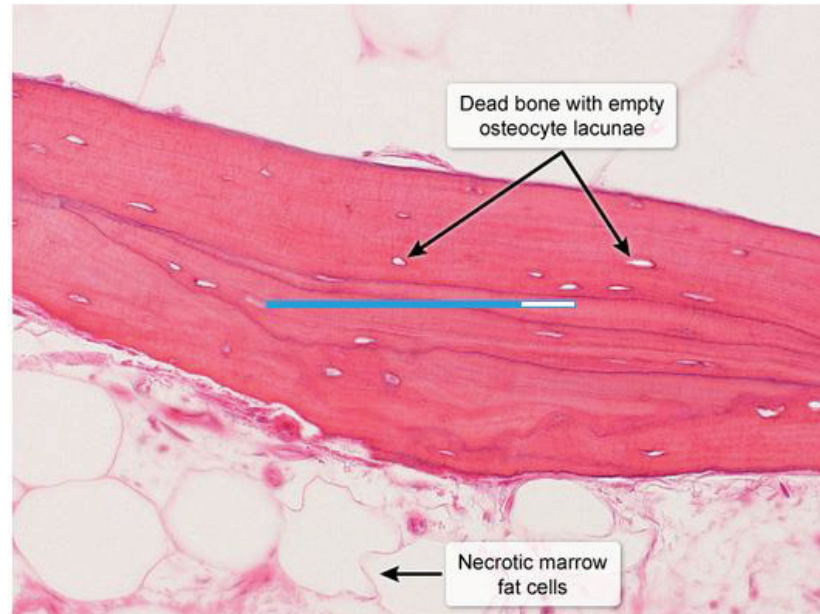


inspection

• Necrosis of surrounding adipocytes

Exhibit Display

Osteonecrosis



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New | Existing

My Notebook



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

with no swelling, erythema, or warmth in the surrounding area. Microscopic analysis of the wedge-shaped zone of affected bone is notable for dead bony trabeculae (empty lacunae) and fat necrosis.

(Choice A) Trochanteric bursitis causes sharp, intermittent pain at the lateral hip and thigh. Pain is increased with pressure on the affected hip (eg, lying on the side) and with walking. Restricted joint movement is not usually found.

(Choice C) Osteoarthritis tends to occur in older patients and is not associated with sickle cell disease. Osteoarthritis causes pain during activity that is relieved by rest. Joint instability and crepitus may be present.

(Choice D) Rheumatoid arthritis tends to affect the smaller joints of the hand and wrist. It causes morning stiffness, spongy synovitis, and joint deformities.

(Choice E) Septic arthritis manifests with acute onset of pain in the joint. Physical examination shows swelling, erythema, and warmth.

Educational objective:

Osteonecrosis (avascular necrosis) occurs due to impaired blood supply to a segment of bone. The femoral head is the most common location. Common causes include sickle cell disease, glucocorticoid therapy, vasculitis, and alcoholism.



1



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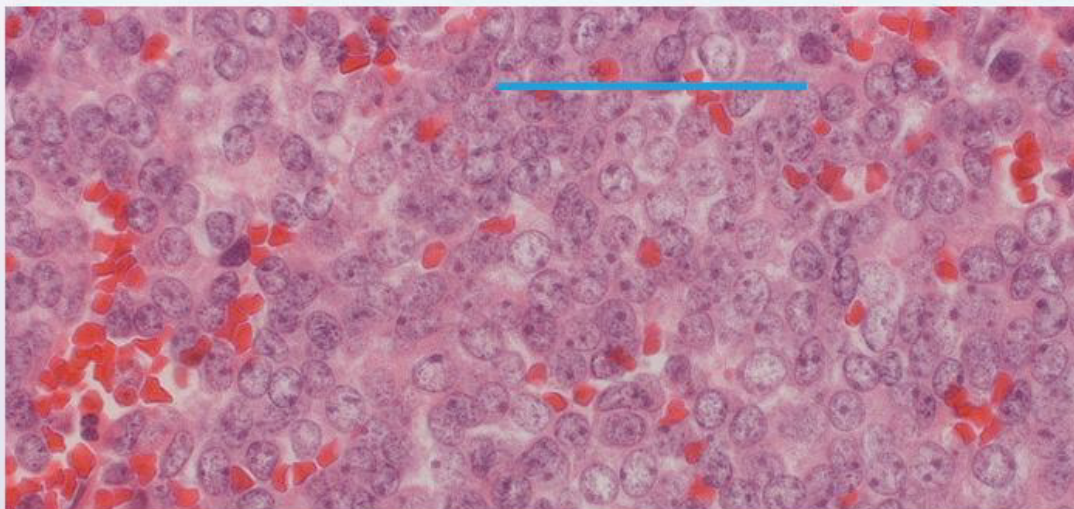


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End Block

A 15-year-old boy is brought to the emergency department due to hemoptysis. He has a history of amputation of the right lower extremity for "bone cancer" in Mexico. Chest imaging reveals a lung mass. Excisional biopsy of the mass shows sheets of uniform, small (slightly larger than lymphocytes), round cells with scant, clear cytoplasm. The cellular deposits are interrupted by vascular fibrous septae, with areas of hemorrhage and an abrupt transition from viable to necrotic cells. A representative sample is shown in the image.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

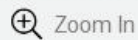
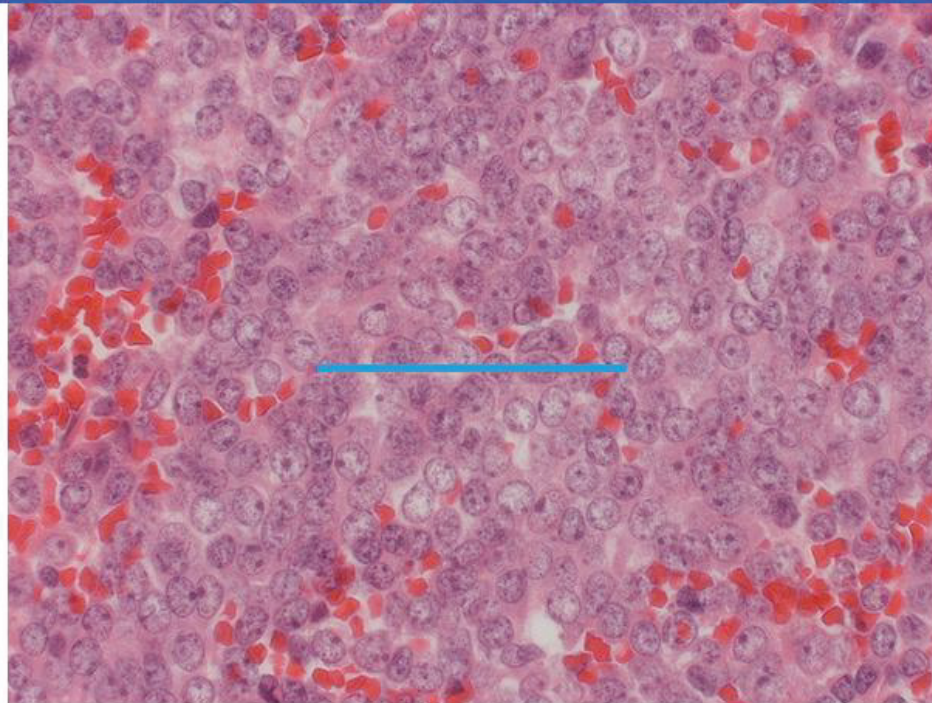


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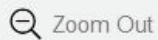


Settings

Exhibit Display



Zoom In



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Reset



New | Existing



My Notebook



2



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

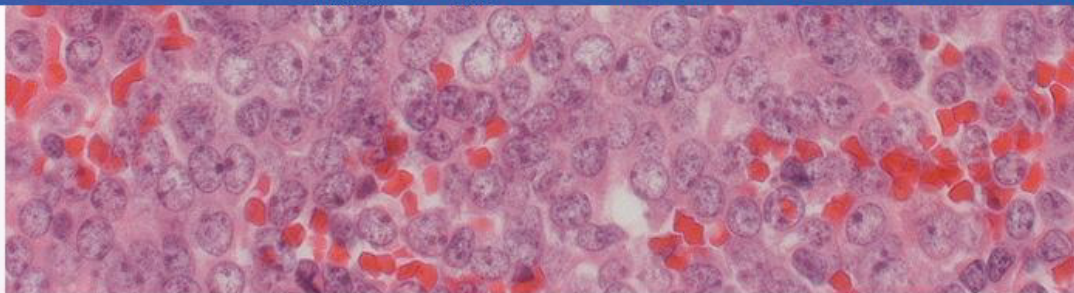
Notes

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Text Zoom

Settings



Which of the following is the most likely diagnosis?

- ☐ A. Adenocarcinoma
- ☐ B. Chondrosarcoma
- ☐ C. Ewing sarcoma
- ☐ D. Multiple myeloma
- ☐ E. Osteosarcoma

Submit

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2



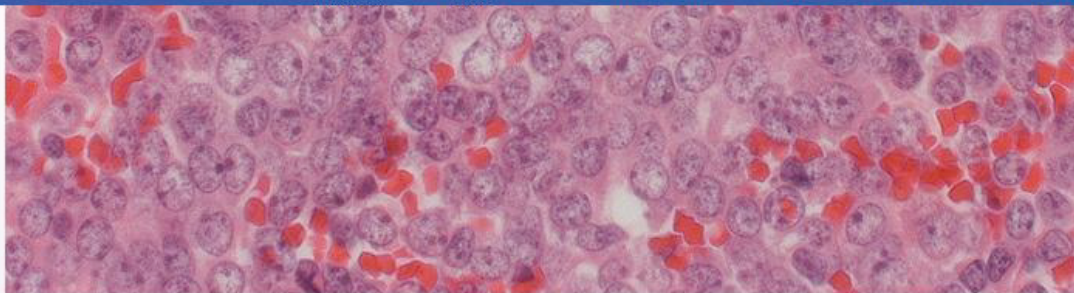
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Which of the following is the most likely diagnosis?

- ☐ A. Adenocarcinoma (5%)
- ☐ B. Chondrosarcoma (7%)
- ☒ C. Ewing sarcoma (61%)
- ☐ D. Multiple myeloma (4%)
- ☐ E. Osteosarcoma (20%)

Correct

61%

11 secs

01/28/2021

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Ewing sarcoma

Epidemiology

- Mesenchymal stem cell neoplasm*
- Primarily seen in children/young adults
- Site of origin: long bones, axial skeleton, or pelvis

Manifestations

- Localized pain & swelling
- Early metastases to lungs & other bones (may be subclinical)

Histopathology

- Sheets of uniform, small, round cells separated by fibrous septae
- Scant, clear cytoplasm (heavy glycogen content)
- Areas of hemorrhage & necrosis
- Rare mitotic figures

*Ewing sarcoma was previously thought to be neuroectodermal in origin.

This boy with a history of bone cancer has a lung tumor with sheets of uniform, small, round cells, raising strong suspicion for metastatic **Ewing sarcoma** (ES). ES is the second most common childhood bone malignancy (after osteosarcoma) and typically presents with pain and swelling at the bone tumor site.

Spread to the lungs or other tissues can occur in those who don't undergo both resection and chemotherapy.



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Spread to the lungs or other tissue can occur in those who don't undergo both resection and chemotherapy.

ES is a primitive, undifferentiated tumor that was originally thought to be neuroectodermal in origin but is now believed to arise from a **mesenchymal stem cell**. Tumor histology typically reveals sheets of **uniform, small, round, cells** with clear, scant cytoplasm separated by **fibrous septae** and patches of necrosis/hemorrhage. This appearance resembles neuroendocrine tumors such as carcinoid and small cell lung cancer. Most cases of ES involve **translocations** of *EWSR1* and *FLI1*.

(Choice A) Adenocarcinoma, the most common primary lung malignancy, often metastasizes to bone. However, histopathology would show **neoplastic glands** lined by mucin-producing cells.

(Choice B) Chondrosarcoma is an uncommon tumor and typically occurs in the 5th or 6th decade of life. Histology shows **neoplastic chondrocytes** in a hyaline cartilage matrix, usually with small calcifications.

(Choice D) Multiple myeloma is a plasma cell malignancy that is extremely rare in patients age <40. X-ray often shows multiple lytic lesions, osteopenia, and pathologic fractures. The malignant cells have **eccentric nuclei with "clock-face" chromatin**, perinuclear clearing, and abundant basophilic cytoplasm.

(Choice E) Osteosarcoma is the most common primary bone malignancy. Histology shows pleomorphic, spindle-shaped cells that produce **new osteoid** and bone.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

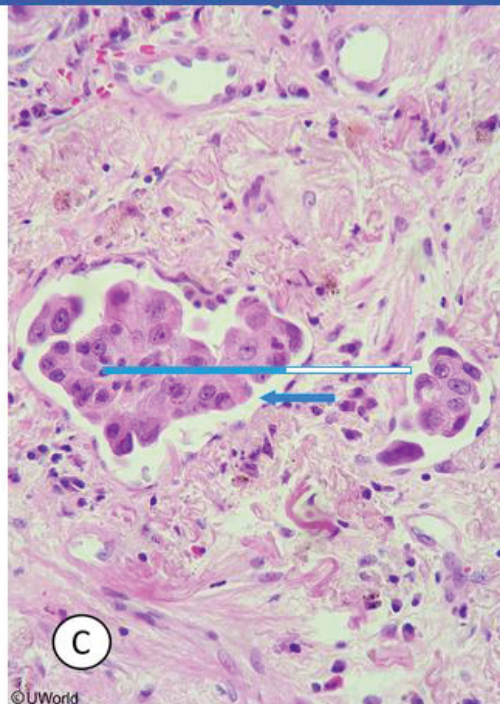
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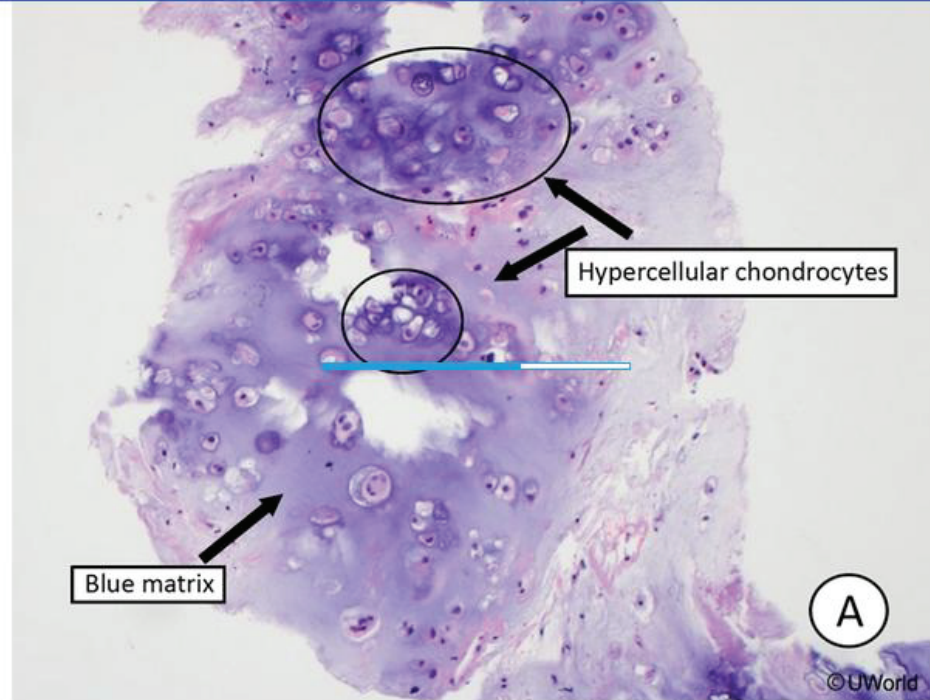


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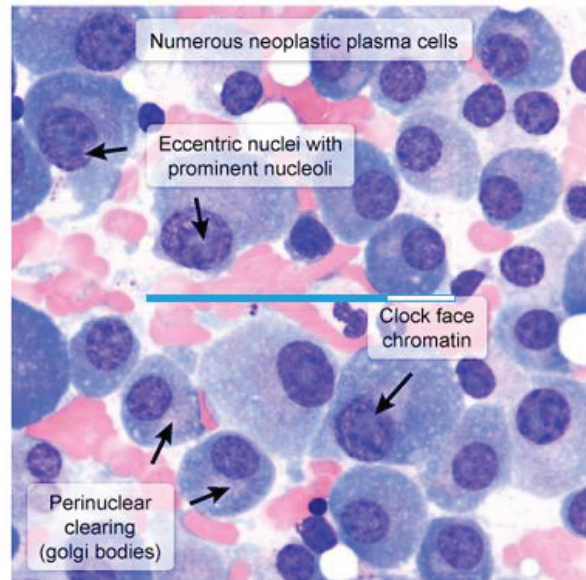
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Plasma cell neoplasm



Multiple myeloma: >10% bone marrow plasma cells

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Zoom In

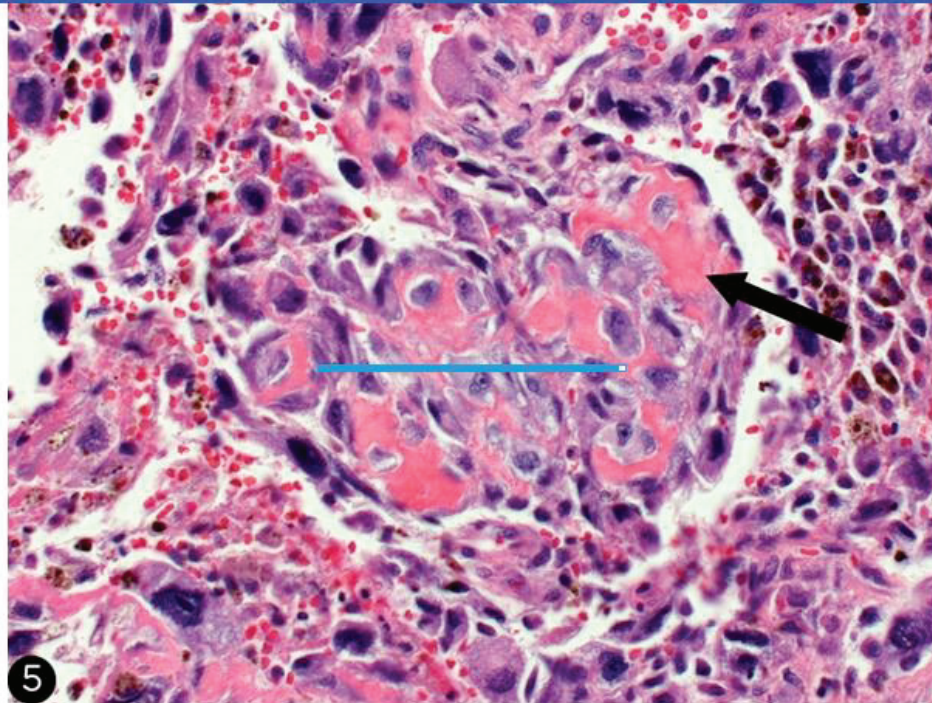
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Reset

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Exhibit Display



Zoom In

Zoom Out

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New | Existing

My Notebook

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(Choice B) Chondrosarcoma is an uncommon tumor and typically occurs in the 5th or 6th decade of life.

Histology shows **neoplastic chondrocytes** in a hyaline cartilage matrix, usually with small calcifications.

(Choice D) Multiple myeloma is a plasma cell malignancy that is extremely rare in patients age <40. X-ray often shows multiple lytic lesions, osteopenia, and pathologic fractures. The malignant cells have **eccentric nuclei with "clock-face" chromatin**, perinuclear clearing, and abundant basophilic cytoplasm.

(Choice E) Osteosarcoma is the most common primary bone malignancy. Histology shows pleomorphic, spindle-shaped cells that produce **new osteoid** and bone.

Educational objective:

Ewing sarcoma is the second most common malignant bone tumor of childhood (after osteosarcoma). It most commonly involves the lower extremity and pelvis and often metastasizes to the lungs.

Histopathology is characterized by uniform, small, round, cells; fibrous septae; and patches of necrosis and hemorrhage.

References

- **Pediatric malignant bone tumors: a review and update on current challenges, and emerging drug targets.**



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

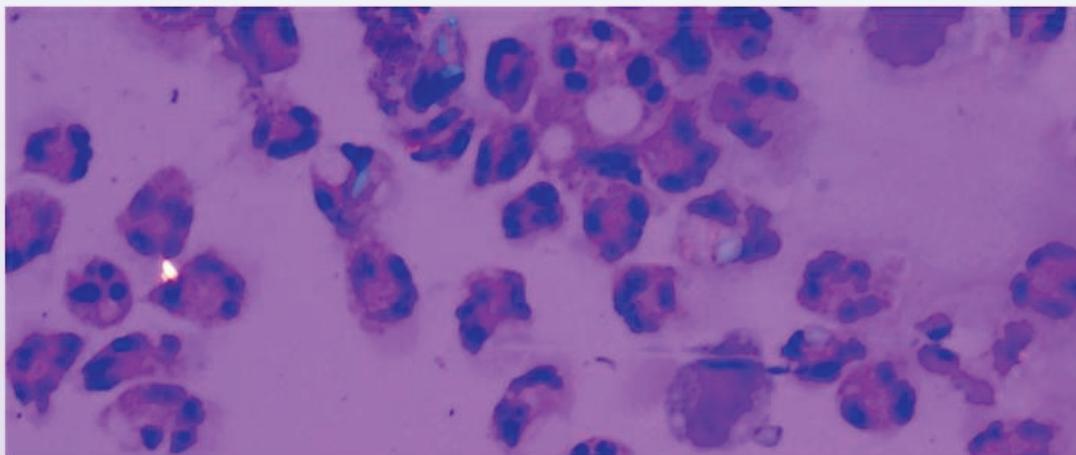


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Settings

A 57-year-old man comes to the emergency department due to a 1-day history of pain and swelling in his right knee. The pain is severe, and he has had difficulty bearing weight on the right leg. He previously felt well. Past medical history is notable for hypertension and seasonal allergies. The patient does not use tobacco and drinks 1 or 2 alcoholic beverages a week. On examination, the right knee is red and swollen. He has pain with passive range of motion at the knee. The knee ligaments show no significant laxity. Synovial fluid obtained from the involved joint shows a white blood cell count of $25,000/\text{mm}^3$, with a neutrophilic predominance, and numerous crystals.



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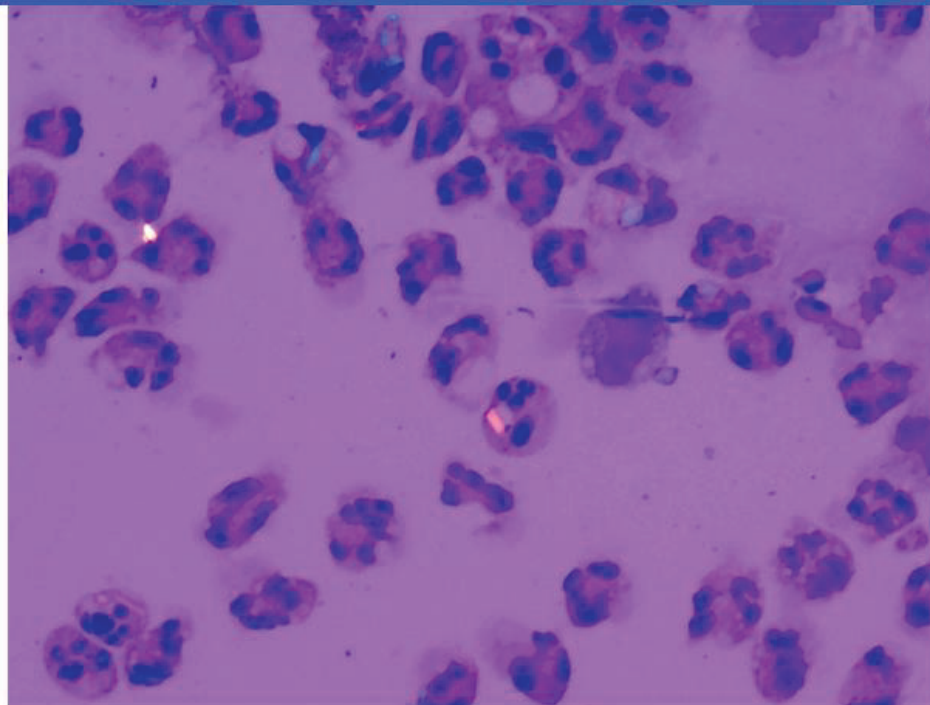


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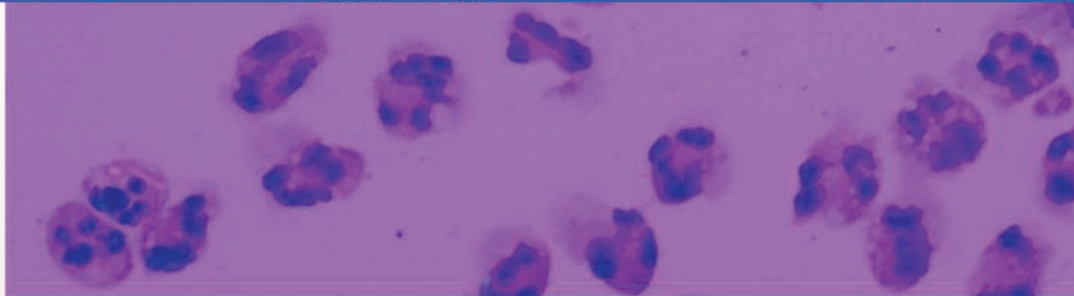


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These crystals are most likely composed of which of the following substances?

- ☐ A. Calcium hydroxyapatite
- ☐ B. Calcium oxalate
- ☐ C. Calcium pyrophosphate
- ☐ D. Cholesterol
- ☐ E. Monosodium urate
- ☐ F. Uric acid



These crystals are most likely composed of which of the following substances?

- ☐ A. Calcium hydroxyapatite (5%)
- ☐ B. Calcium oxalate (6%)
- ☒ C. Calcium pyrophosphate (56%)
- ☐ D. Cholesterol (0%)
- ☐ E. Monosodium urate (19%)
- ☐ F. Uric acid (11%)

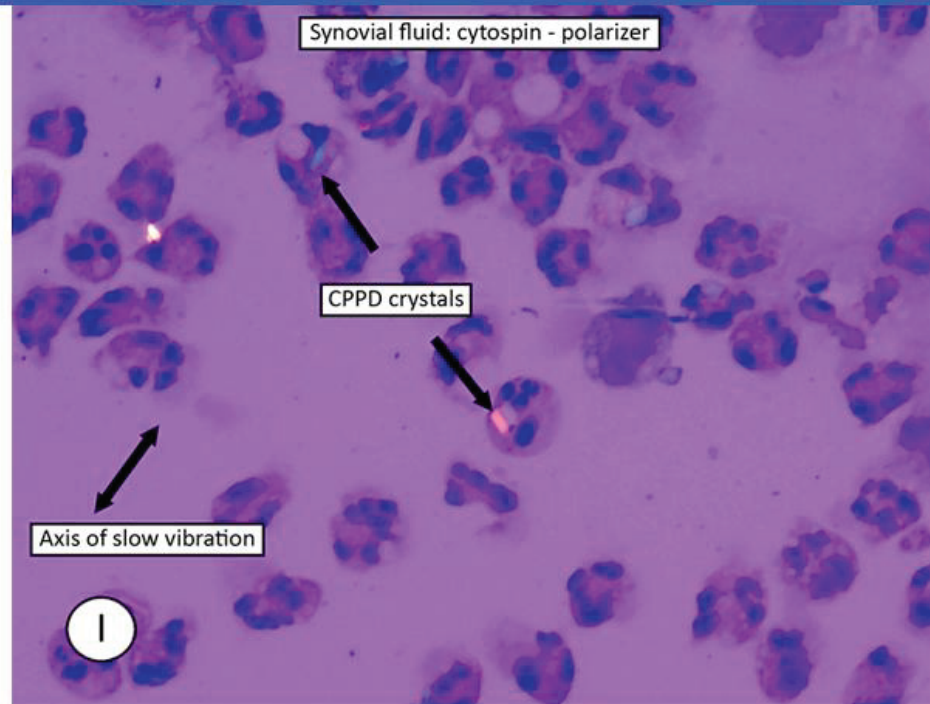
Correct

56%

23 secs

10/11/2020

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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Pseudogout, or calcium pyrophosphate deposition disease (CPPD), results from accumulation of calcium pyrophosphate crystals in the synovial fluid. Patients present with an acute mono- or oligoarticular arthritis characterized by pain, joint swelling, erythema, and warmth. Pseudogout and gout can be difficult to distinguish clinically. The knee joint is involved in >50% of pseudogout cases, whereas the first metatarsophalangeal joint is more frequently involved in gout.

In pseudogout, synovial fluid analysis reveals an elevated white blood cell count with neutrophilic predominance. Identification of **rhomboid-shaped calcium pyrophosphate crystals** is diagnostic. These crystals are positively birefringent under polarized light, meaning that the color pattern is the opposite of that seen in gout. Pseudogout crystals are blue when aligned parallel and yellow when aligned perpendicular to the slow ray of the compensator.

(Choice A) Calcific tendonitis results from the deposition of calcium hydroxyapatite crystals in periarticular soft tissues (especially tendons). The rotator cuff tendons are most commonly affected.

(Choice B) **Calcium oxalate** is one of the most common constituents of renal calculi.

(Choice D) Soft-tissue deposits of cholesterol and other lipids are called xanthomas. These appear as yellow papules on the knees, elbows, and tendon insertion sites in patients with hyperlipidemia.



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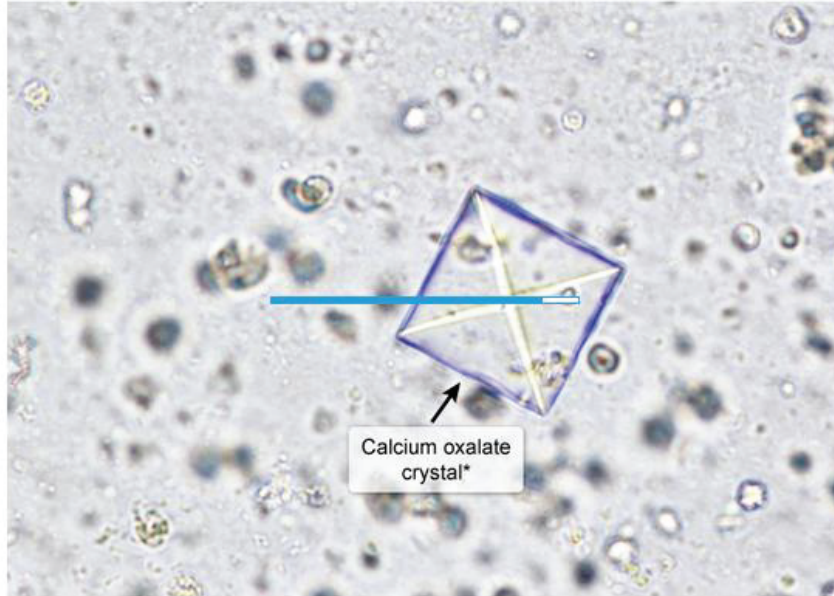
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Calcium oxalate crystals



***"Envelope-shaped" crystal

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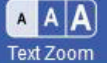
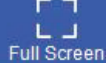
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Zoom Out

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New | Existing

My Notebook



perpendicular to the slow ray of the compensator.

(Choice A) Calcific tendonitis results from the deposition of calcium hydroxyapatite crystals in periarticular soft tissues (especially tendons). The rotator cuff tendons are most commonly affected.

(Choice B) Calcium oxalate is one of the most common constituents of renal calculi.

(Choice D) Soft-tissue deposits of cholesterol and other lipids are called xanthomas. These appear as yellow papules on the knees, elbows, and tendon insertion sites in patients with hyperlipidemia.

(Choices E and F) In gout, monosodium urate (the salt of uric acid) is deposited in joints and soft tissues. Urate crystals are needle-shaped and negatively birefringent.

Educational objective:

Synovial fluid analysis showing rhomboid-shaped calcium pyrophosphate crystals is diagnostic of pseudogout. These crystals are positively birefringent under polarized light. The knee joint is involved in >50% of cases.

References

- Calcium pyrophosphate dihydrate and basic calcium phosphate crystal-induced arthropathies: update on pathogenesis, clinical features, and therapy.





Mark

Previous

Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



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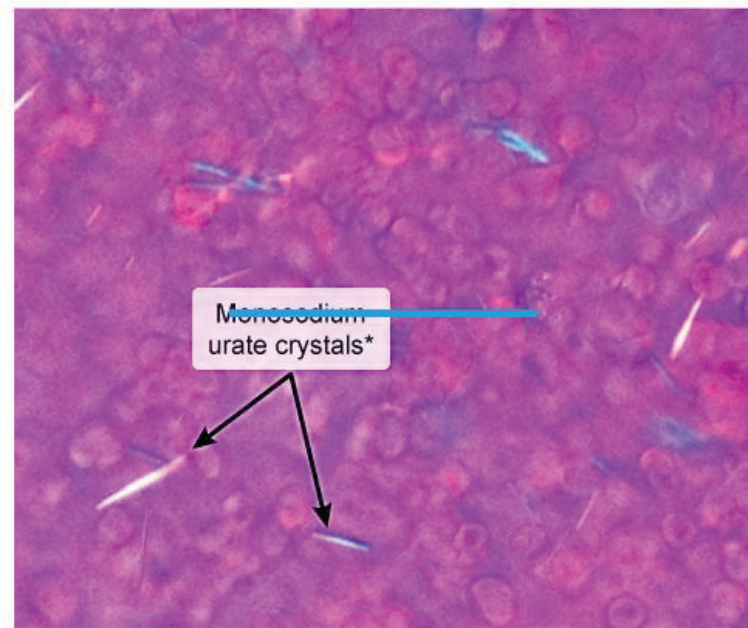


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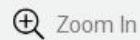
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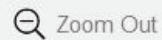
Gout



*Needle-shaped, negatively birefringent crystals under polarized light



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New | Existing



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End Block



A 45-year-old man comes to the office due to right ankle pain for the past 2 days. The patient was running downhill on a dirt trail when he twisted his ankle inward. Since then, he has had pain and swelling at the right ankle but is able to walk unassisted. The patient has no other medical conditions and takes no chronic medications. On examination, there is bluish discoloration over the lateral aspect of the joint. He has maximal tenderness to palpation at the anterolateral aspect of the ankle joint. Forced inversion of the foot also increases the pain. Which of the following structures is most likely injured in this patient?

- ☐ A. Achilles tendon
- ☐ B. Deltoid ligament
- ☐ C. Subtalar joint
- ☐ D. Talofibular ligament
- ☐ E. Tibiofibular ligament

Submit



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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A 45-year-old man comes to the office due to right ankle pain for the past 2 days. The patient was running downhill on a dirt trail when he twisted his ankle inward. Since then, he has had pain and swelling at the right ankle but is able to walk unassisted. The patient has no other medical conditions and takes no chronic medications. On examination, there is bluish discoloration over the lateral aspect of the joint. He has maximal tenderness to palpation at the anterolateral aspect of the ankle joint. Forced inversion of the foot also increases the pain. Which of the following structures is most likely injured in this patient?

- ☐ A. Achilles tendon (1%)
- ☐ B. Deltoid ligament (6%)
- ☐ C. Subtalar joint (2%)
- ☒ D. Talofibular ligament (80%)
- ☐ E. Tibiofibular ligament (8%)

Correct



80%

Answered correctly



52 secs

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11/27/2020

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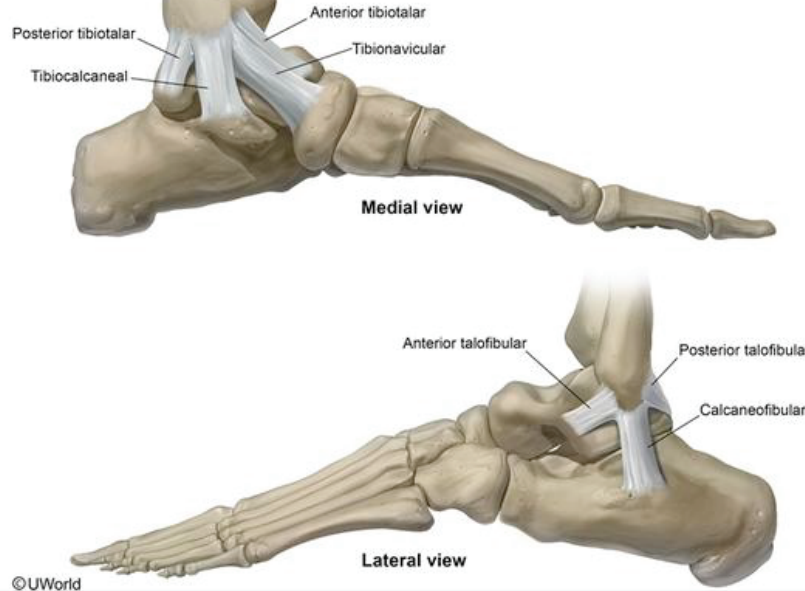
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Ankle ligaments



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Zoom Out

Reset

New | Existing

My Notebook

This patient has a right lateral **ankle sprain**, which is most often due to inversion of a plantar-flexed foot. The ankle is stabilized laterally by the anterior inferior tibiofibular, anterior talofibular, posterior talofibular, and calcaneofibular ligaments.

The lateral ankle ligaments are weaker and are injured more often than the medial ligaments. The most common ankle sprains involve only the **anterior talofibular ligament** and present with pain and ecchymosis at the **anterolateral aspect** of the ankle. However, stronger forces can injure multiple ligaments, leading to significant joint instability with possible nerve injury and joint dislocation/fracture.

(Choice A) The soleus and gastrocnemius muscles combine to form the Achilles tendon, which inserts on the posterior calcaneus and acts in ankle flexion. The tendon can be injured with sudden forces during strenuous activities (eg, sudden pivoting on a foot or rapid acceleration).

(Choice B) The medial deltoid ligament complex is stronger than the other ligaments and is not commonly injured. Forced eversion of the ankle can damage the deltoid ligament but more commonly causes an avulsion fracture of the medial malleolus.

(Choice C) The subtalar joint is at the posterior junction between the talus and the calcaneus and is reinforced by the talocalcaneal ligaments. The joint is involved with inversion, eversion, dorsiflexion, and



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice B) The medial deltoid ligament complex is stronger than the other ligaments and is not commonly injured. Forced eversion of the ankle can damage the deltoid ligament but more commonly causes an avulsion fracture of the medial malleolus.

(Choice C) The subtalar joint is at the posterior junction between the talus and the calcaneus and is reinforced by the talocalcaneal ligaments. The joint is involved with inversion, eversion, dorsiflexion, and plantar flexion of the foot, but is infrequently injured.

(Choice E) Dorsiflexion and/or eversion of the ankle can cause a high ankle sprain affecting the syndesmotic structures (interosseous membrane and anterior, posterior, and transverse tibiofibular ligaments), which connect the tibia and fibula. Injury to these structures is uncommon as they can withstand severe forces. Patients usually have an unstable ankle joint with tenderness at the distal tibiofibular joint, but no significant swelling.

Educational objective:

Lateral ankle sprain is due to inversion of a plantar-flexed foot and most commonly involves the anterior talofibular ligament. Stronger forces can cause joint instability by injuring additional ligaments.

References

- [Ankle sprains and instability.](#)



1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 48-year-old woman comes to the emergency department due to back pain after minor trauma. She has no leg weakness or numbness. Review of systems is positive for recent-onset hot flashes and irregular menses; her most recent menstruation was 2 weeks ago. The patient has a long history of hypothyroidism treated with levothyroxine and rheumatoid arthritis treated with methotrexate. She has also taken oral prednisone for frequent symptom flares. The patient does not use tobacco, alcohol, or illicit drugs, and she consumes a balanced diet. Physical examination shows point tenderness over the midthoracic spine. The straight-leg raising test is negative, and neurologic examination of the lower extremities shows no abnormalities. Spine imaging is shown below:



1



Feedback



Suspend



End Block

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



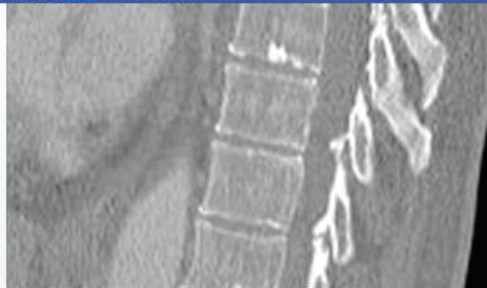
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Which of the following contributed most to this patient's current condition?

- ☐ A. Inadequate levothyroxine replacement
- ☐ B. Medication adverse effect
- ☐ C. Nutritional vitamin deficiency
- ☐ D. Ovarian hormone deficiency
- ☒ E. Vertebral joint inflammation

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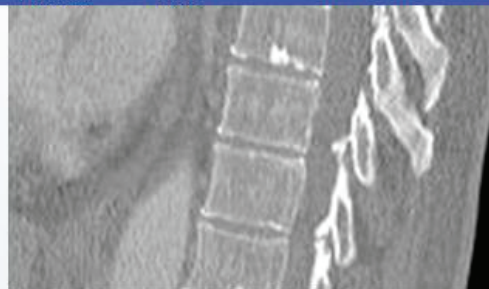
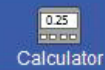
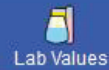
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Which of the following contributed most to this patient's current condition?

- ☐ A. Inadequate levothyroxine replacement (2%)
- ☒ B. Medication adverse effect (68%)
- ☐ C. Nutritional vitamin deficiency (2%)
- ☐ D. Ovarian hormone deficiency (21%)
- ☐ E. Vertebral joint inflammation (5%)

Correct



68%



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11/30/2020

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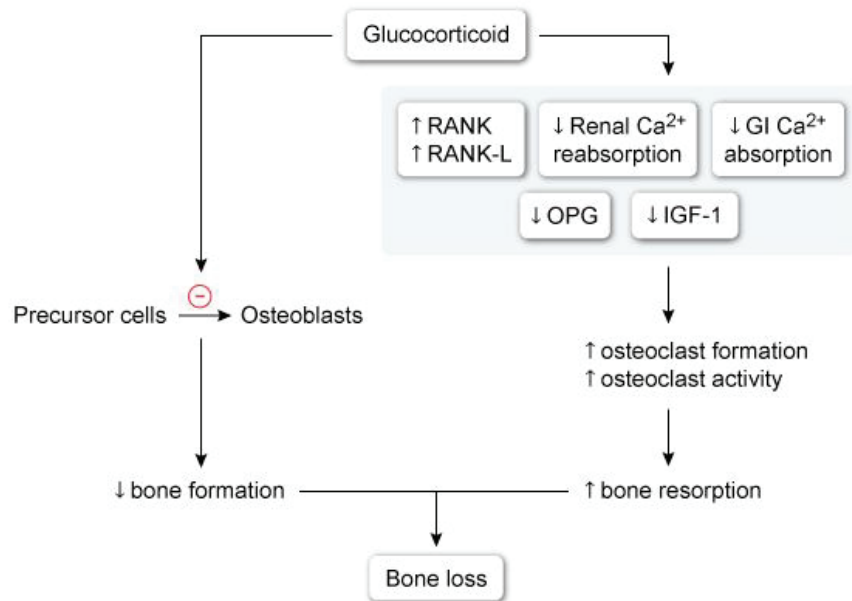
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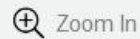
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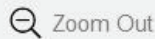
Glucocorticoid effect on bone



OPG = osteoprotegerin; RANK = receptor activator of nuclear factor kappa B;



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Zoom Out



Reset



New | Existing



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OPG = osteoprotegerin; RANK = receptor activator of nuclear factor kappa B;





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

OPG = osteoprotegerin; RANK = receptor activator of nuclear factor kappa B;
RANK-L = RANK ligand; GI = gastrointestinal; IGF-1 = insulin-like growth factor-1

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This patient has a **fragility fracture** of a thoracic vertebra (ie, fracture due to a force significantly less than that required to fracture a normal bone). A fragility fracture suggests underlying bone pathology, often due to metastatic malignancy or intrinsic bone disease. In this patient, who has had frequent exposure to systemic glucocorticoids (eg, prednisone), this likely represents **osteoporosis**.

Chronic or recurrent **glucocorticoid use**, as is occasionally needed for patients with rheumatoid arthritis, is associated with an increased risk for osteoporosis. Osteoporosis can also occur due to systemic absorption of topical glucocorticoids (eg, inhaled glucocorticoids used in the treatment of asthma). Glucocorticoids promote osteoporosis by inhibiting proliferation and differentiation of osteoblast precursor cells, promoting osteoclast differentiation and activity, and suppressing intestinal calcium absorption and renal calcium reabsorption.

(Choice A) **Thyroid hormone** stimulates osteoclast differentiation and activity, bone resorption, and release of calcium into circulation. Thyrotoxic states (eg, excessive levothyroxine dose, endogenous hyperthyroidism) cause increased bone turnover with net bone loss. However, inadequate levothyroxine dosing is not a significant contributor to bone loss.

(Choice C) Deficiency of vitamin D can lead to osteoporosis. Risk factors include malabsorption

Block Time Remaining: 00:42:59

TUTOR

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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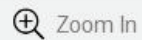
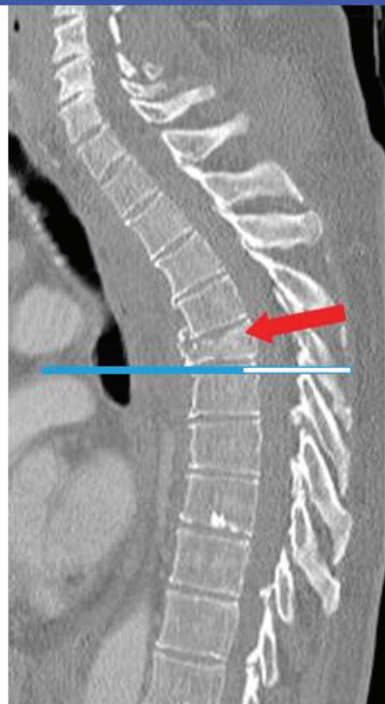


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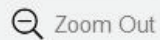


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New | Existing



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(Choice C) Deficiency of vitamin D can lead to osteoporosis. Risk factors include malabsorption.

Block Time Remaining: 00:42:59

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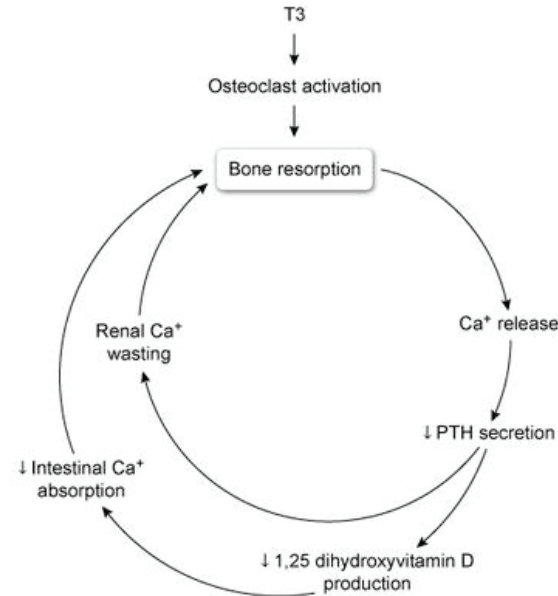
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Hyperthyroid-induced bone loss



PTH = Parathyroid hormone.

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New | Existing

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(Choice C) Deficiency of vitamin D can lead to osteoporosis. Risk factors include malabsorption.

Block Time Remaining: 00:42:59

TUTOR

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

(Choice C) Deficiency of vitamin D can lead to osteoporosis. Risk factors include malabsorption syndromes (eg, celiac disease) and lack of sun exposure, but nutritional deficiency is not a common cause of vitamin D deficiency. Glucocorticoid use is likely a more significant factor in this patient.

(Choice D) Loss of ovarian estrogen production after menopause leads to an increased risk of osteoporosis. However, postmenopausal osteoporosis develops slowly, and fracture is uncommon until at least 10-15 years after cessation of menses; this patient is still perimenopausal, and loss of estrogen is unlikely to have caused her osteoporosis.

(Choice E) Involvement of the cervical spine is common in rheumatoid arthritis and, over time, can lead to atlantoaxial instability, subluxation with possible cord compression, and odontoid fracture. However, involvement of the thoracic and lumbar spine is uncommon.

Educational objective:

Osteoporosis is a common cause of fragility fractures, which occur in the absence of significant trauma. Chronic or recurrent use of glucocorticoids (eg, prednisone) promotes osteoporosis and increases the risk of fractures.

Pharmacology

Rheumatology/Orthopedics & Sports

Corticosteroids



1



Feedback



Suspend



End Block



A 36-year-old construction worker comes to the emergency department after falling 3 meters (~10 ft) from a ladder. The patient braced his fall with outstretched hands and experienced severe pain in the left wrist immediately on impacting the ground. On examination, the left wrist is swollen, with no lacerations. A strong radial pulse is present, and the fingers are well perfused. There is a palpable mass just proximal to the left palm. X-ray of the left wrist reveals a lunate dislocation without evidence of a distal radius fracture, as seen in the [exhibit](#). The patient is at greatest risk for impairment of which of the following hand functions?

- ☐ A. Finger abduction
- ☐ B. Finger interphalangeal joint flexion
- ☐ C. Thumb abduction
- ☒ D. Thumb adduction
- ☐ E. Thumb extension

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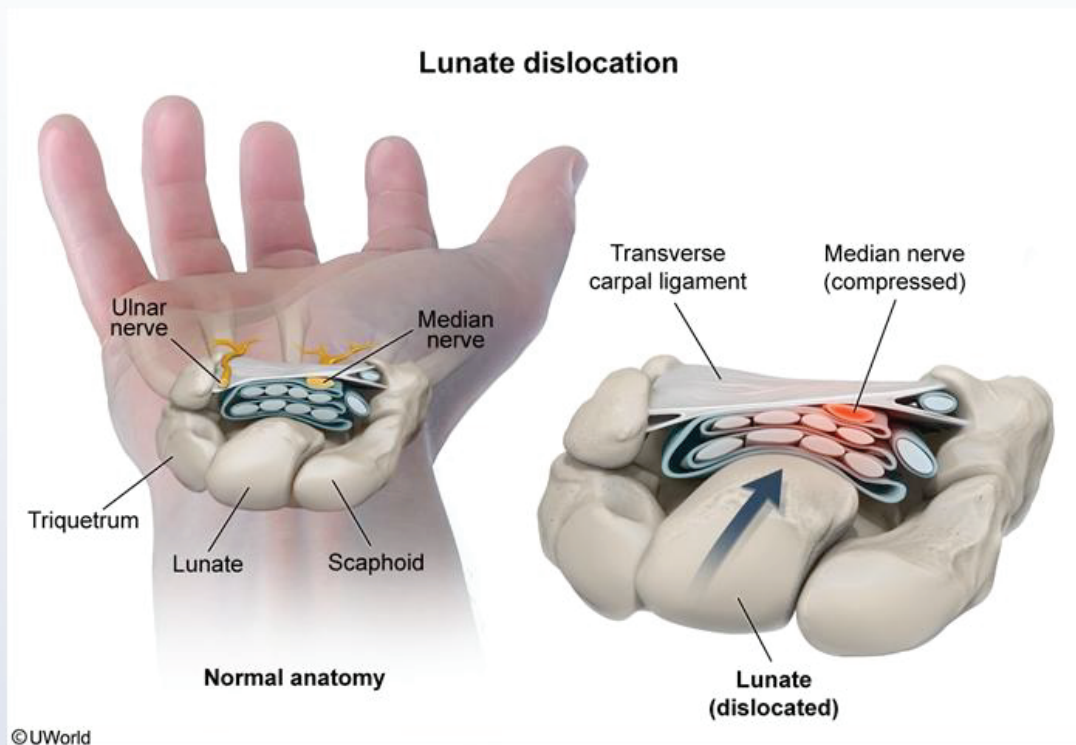
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New | Existing

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A 36-year-old **construction worker** comes to the emergency department after falling 3 meters (~10 ft) from a ladder. The patient braced his fall with **outstretched hands** and experienced severe pain in the **left wrist** immediately on impacting the ground. On examination, the left wrist is swollen, with no lacerations. A strong radial pulse is present, and the fingers are well perfused. There is a palpable mass just **proximal** to the **left palm**. X-ray of the left wrist reveals a **lunate dislocation** without evidence of a distal radius fracture, as seen in the **exhibit**. The patient is at greatest risk for impairment of which of the following hand functions?

- ☐ A. Finger abduction (9%)
- ☐ B. Finger interphalangeal joint flexion (17%)
- ☒ C. Thumb abduction (41%)
- ☐ D. Thumb adduction (23%)
- ☐ E. Thumb extension (8%)



This patient who experienced a high-energy fall onto an outstretched hand now has a **volar lunate**

This patient who experienced a high-energy fall onto an outstretched hand now has a **volar lunate dislocation**, with the displaced lunate now palpable in the patient's proximal palm and visualized on lateral x-ray of the wrist ("**spilled teacup**" sign).

Lunate dislocation requires a high-energy force to disrupt the numerous ligaments (eg, scapholunate, capitolunate, lunotriquetral) that typically stabilize the lunate. When severe ligamentous injury occurs, the lunate can dislocate volarly from its normal position within the floor of the **carpal tunnel** and **compress** and/or injure the **median nerve**.

Median nerve injury at the level of the carpal tunnel may result in both sensory and **motor deficits** in the distribution of the median nerve's distal branches:

- Palmar digital branches: numbness, pain, and/or paresthesia in the palmar surface of the first 3½ digits; weakness of the first and second lumbrical muscles (interphalangeal joint extension)
- Recurrent branch of the median nerve to the **thenar muscles**: **weakness** of the abductor pollicis brevis (**thumb abduction**), flexor pollicis brevis (thumb flexion), and opponens pollicis (thumb opposition)

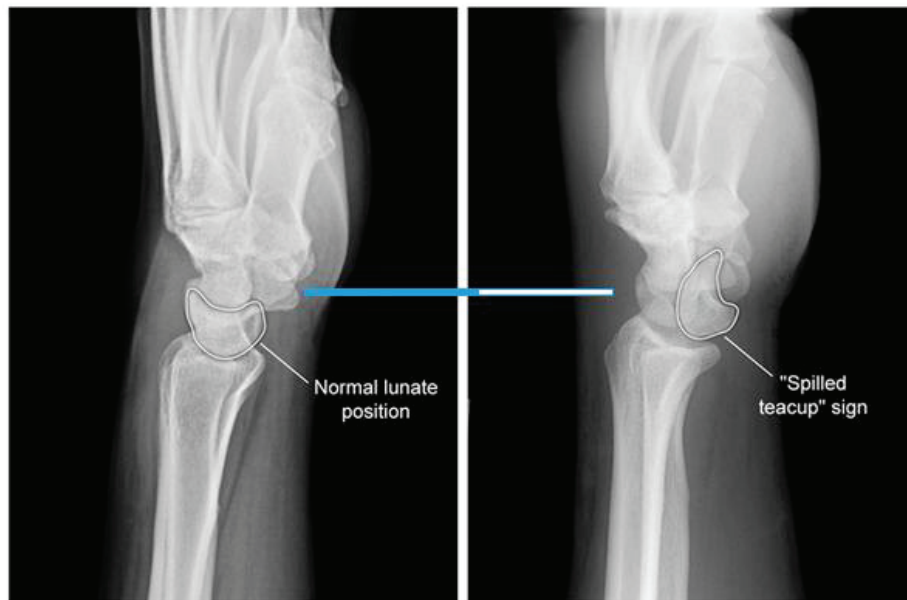
Prompt reduction of the dislocated lunate is required to prevent permanent damage to the median nerve.

(Choices A and D) The deep motor branch of the ulnar nerve is responsible for both finger abduction due

This patient who experienced a high-energy fall onto an outstretched hand now has a volar lunate

Exhibit Display

Volar lunate dislocation



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Zoom In

Zoom Out

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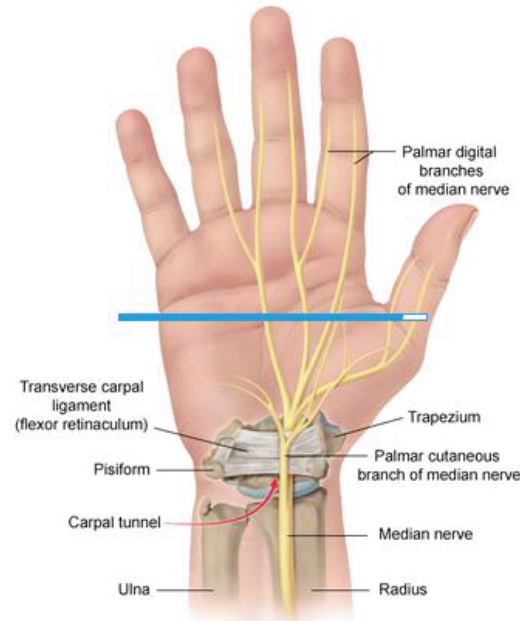
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This patient who experienced a high-energy fall onto an outstretched hand now has a **volar lunate**

Exhibit Display

Carpal tunnel, palmar view



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(Choices A and D) The deep motor branch of the ulnar nerve is responsible for both finger abduction due

(Choices A and D) The deep motor branch of the ulnar nerve is responsible for both finger abduction due to innervation of the dorsal and volar interossei and thumb adduction due to innervation of the adductor pollicis. The ulnar nerve is susceptible to acute compression at the wrist (ie, **Guyon canal syndrome**) when the hook of the hamate is fractured.

(Choice B) Branches of the median and ulnar nerves in the forearm innervate the flexor digitorum superficialis and profundus muscles that control finger interphalangeal joint flexion. These branches arise and innervate their respective muscles prior to the carpal tunnel and Guyon canal and would not be affected by wrist trauma.

(Choice E) The radial nerve innervates the extensor pollicis longus and brevis, which control thumb extension. All radial nerve-innervated muscles are located proximal to the wrist and therefore would not be affected by lunate dislocation.

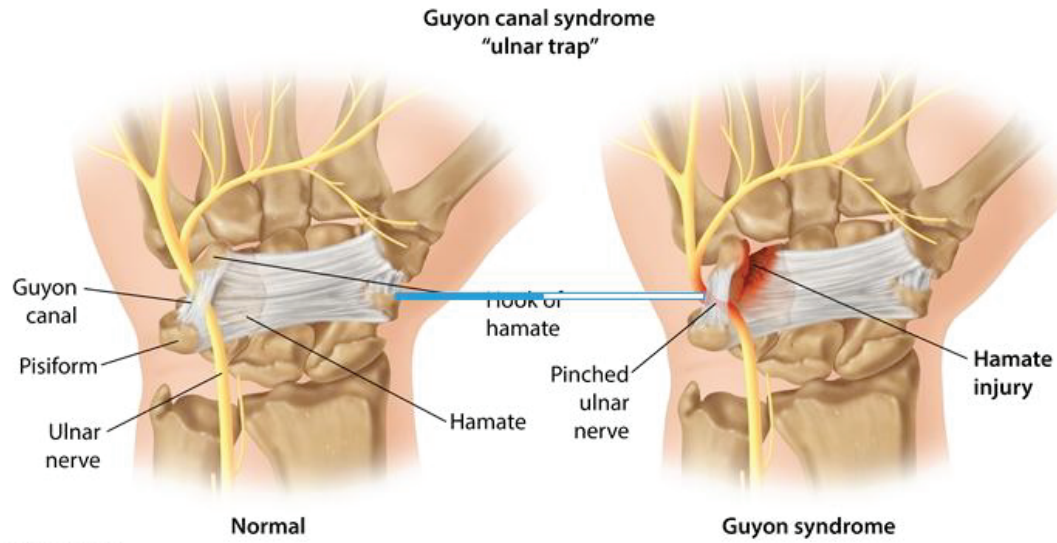
Educational objective:

Volar dislocation of the lunate from its normal position within the floor of the carpal tunnel can cause median nerve compression and/or injury. Median nerve injury at the level of the carpal tunnel may result in weakness of thumb abduction, flexion, and opposition.

References

(Choices A and D) The deep motor branch of the ulnar nerve is responsible for both finger abduction and

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 45-year-old woman comes to the clinic with a 3-month history of persistent shoulder and back pain and easy fatigability. She also has pain and stiffness in all her muscles that worsens in the morning and evening. She does not participate in any regular exercise because her pain is exacerbated with activity. She works as a computer programmer and reports some difficulty concentrating on her job. Past medical history is significant for depression and gastroesophageal reflux disease, but she is not currently taking any medications. Physical examination shows normal range of motion and 5/5 muscle strength in both upper and lower extremities. Soft tissue tenderness is present at several locations bilaterally above and below the waist. Which of the following is the most likely diagnosis?

- ☐ A. Ankylosing spondylitis
- ☐ B. Dermatomyositis
- ☐ C. Fibromyalgia
- ☐ D. Polymyalgia rheumatica
- ☐ E. Rheumatoid arthritis



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Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



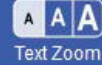
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Calculator



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Text Zoom



Settings

easy fatigability. She also has pain and stiffness in all her muscles that worsens in the morning and evening. She does not participate in any regular exercise because her pain is exacerbated with activity. She works as a computer programmer and reports some difficulty concentrating on her job. Past medical history is significant for depression and gastroesophageal reflux disease, but she is not currently taking any medications. Physical examination shows normal range of motion and 5/5 muscle strength in both upper and lower extremities. Soft tissue tenderness is present at several locations bilaterally above and below the waist. Which of the following is the most likely diagnosis?

- ☐ A. Ankylosing spondylitis (2%)
- ☐ B. Dermatomyositis (2%)
- ☒ C. Fibromyalgia (71%)
- ☐ D. Polymyalgia rheumatica (20%)
- ☐ E. Rheumatoid arthritis (2%)

Correct

 71%
Answered correctly 02 mins, 34 secs
Time Spent 01/17/2021
Last Updated

Block Time Remaining: 00:48:00

TUTOR

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Clinical features of fibromyalgia

| | |
|-----------------------------|---|
| Symptoms | <ul style="list-style-type: none">• Widespread musculoskeletal pain• Fatigue• Impaired attention & concentration• Psychiatric disturbances (eg, depression, anxiety)• Symptoms lasting for ≥ 3 months |
| Physical examination | <ul style="list-style-type: none">• Multiple tender points at characteristic locations• Absence of joint or muscle inflammation |
| Laboratory findings | <ul style="list-style-type: none">• Normal acute phase reactants (eg, ESR, CRP) & other inflammatory markers |
| Treatment | <ul style="list-style-type: none">• Progressive exercise regimen• Medications: tricyclic antidepressants, cyclic skeletal muscle relaxants, serotonin-norepinephrine reuptake inhibitors |

CRP = C-reactive protein; **ESR** = erythrocyte sedimentation rate.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Fibromyalgia is a chronic disorder that is characterized by **widespread musculoskeletal pain** in association with **fatigue** and neuropsychiatric disturbances (eg, paresthesias, poor sleep, depression, difficulty concentrating). It is most common in women age 20-55. Examination often shows tenderness at characteristic locations in the soft tissues and at bony prominences. The diagnosis can be made in patients with chronic pain and fatigue for >3 months in the absence of physical or laboratory findings suggestive of an inflammatory etiology (eg, synovial swelling, elevated erythrocyte sedimentation rate or C-reactive protein) or other chronic pain syndrome.

The precise etiology of fibromyalgia is unknown, but it likely involves **abnormal central processing** of painful stimuli. Possible contributing factors include genetic predisposition and physical or emotional stressors. Although exercise can temporarily exacerbate the pain of fibromyalgia, gradual **incremental aerobic exercise** is proven to reduce pain and improve function. Tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors modify processing of pain signals and can also be considered in patients with more severe or refractory symptoms.

(Choice A) Ankylosing spondylitis is a chronic inflammatory disease of the axial skeleton characterized by progressive pain and stiffness of the spine, sacroiliitis, and positive serology for HLA-B27 in the majority of patients.



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

patients.

(Choice B) Dermatomyositis is an autoimmune condition that causes bilateral proximal muscle weakness associated with violaceous eruption on the eyelids and knuckles, and elevated creatine kinase levels.

(Choice D) Polymyalgia rheumatica (PMR) is an inflammatory disorder that affects patients age ≥ 50 and causes subacute pain and stiffness in the shoulders and hips, weight loss, fever, and malaise. This patient's age, soft tissue tenderness, and neuropsychiatric symptoms are not consistent with PMR but are typical of fibromyalgia.

(Choice E) Rheumatoid arthritis causes a symmetric, inflammatory polyarthritis. It typically presents with pain and morning stiffness of the metacarpophalangeal and proximal interphalangeal joints. The affected joints are warm, swollen, and tender on palpation.

Educational objective:

Fibromyalgia occurs most commonly in women age 20-55 and presents with diffuse musculoskeletal pain, fatigue, and neuropsychiatric disturbances. It is characterized by abnormal central processing of painful stimuli. Although initially painful, aerobic exercise helps to improve pain and functioning in these patients.

References

- [Fibromyalgia syndrome: etiology, pathogenesis, diagnosis, and treatment.](#)



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Feedback

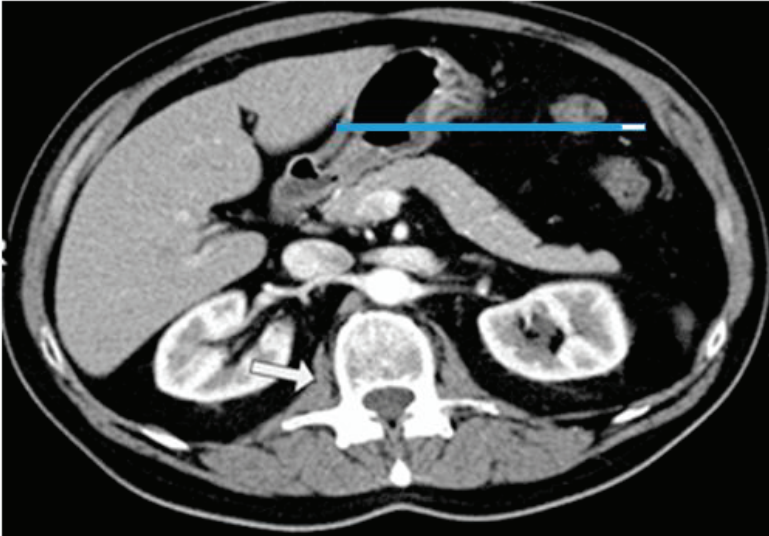


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End Block

A 52-year-old man comes to the hospital following 4 weeks of vague back and abdominal pain. He also has experienced episodic fever, anorexia, and a 2-kg (4.4-lb) weight loss. The patient was recently diagnosed with HIV and has not yet begun taking antiretroviral therapy. He has a history of intravenous drug use. A CT scan of the abdomen reveals an infection involving the structure indicated by the arrow in the image below.



- 1
- 2
- 3
- 4
- 5



Item 1 of 5

Question Id: 1885



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following structures is involved by this patient's infectious process?

- ☐ A. Erector spinae muscle
- ☐ B. Iliacus muscle
- ☐ C. Ligamentum flavum
- ☐ D. Psoas muscle
- ☒ E. Transversus abdominis muscle

Submit

Block Time Remaining: 00:00:07

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End Block



Which of the following structures is involved by this patient's infectious process?

- ☐ A. Erector spinae muscle
- ☐ B. Iliacus muscle
- ☐ C. Ligamentum flavum
- ☐ D. Psoas muscle
- ☐ E. Transversus abdominis muscle

Submit



Which of the following structures is involved by this patient's infectious process?

- ☐ A. Erector spinae muscle (13%)
- ☐ B. Iliacus muscle (7%)
- ☐ C. Ligamentum flavum (3%)
- ☒ D. Psoas muscle (75%)
- ☐ E. Transversus abdominis muscle (0%)

Correct



75%

Answered correctly



44 secs

Time Spent



11/09/2020

Last Updated

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Feedback



Suspend



End Block

- 1
- 2
- 3
- 4
- 5



Item 1 of 5

Question Id: 1885



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Block Time Remaining: 00:00:44

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Feedback



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End Block



The arrow points to a bilaterally symmetric structure that lies in close association to the vertebral body and vertebral transverse process. This is the **psoas muscle**, which originates from the anterior surface of the transverse processes and lateral surface of the vertebral bodies at T12-L5. Inferiorly (at around the level of the inguinal ligament), the psoas muscle combines with the iliacus muscle (**Choice B**) to form the **iliopsoas muscle**, which functions in hip flexion and contributes to external rotation of the thigh.

Psoas abscess can develop due to hematogenous seeding from a distal site (primary abscess) or contiguous spread of infection from adjacent structures such as the vertebra (secondary abscess). Patients often present subacutely with abdominal/flank pain, fever, and inguinal mass. **HIV infection**, intravenous drug use, and diabetes mellitus are risk factors for primary psoas abscess development.

(Choice A) The erector spinae is a large muscle group of the back that courses longitudinally along the spinous processes. Bilateral contraction causes spine extension.

(Choice C) The **ligamenta flava** are paired elastic ligaments that connect the vertebral laminae. The ligamenta flava form the posterior wall of the spinal canal and help stabilize the spine.

(Choice E) The transversus abdominis (transversalis) muscle is the most internal of the **anterior abdominal wall muscles**. It lies immediately deep to the internal oblique and helps to flex the trunk as well as increase intraabdominal pressure during forced expiration.



- 1
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Item 1 of 5

Question Id: 1885



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



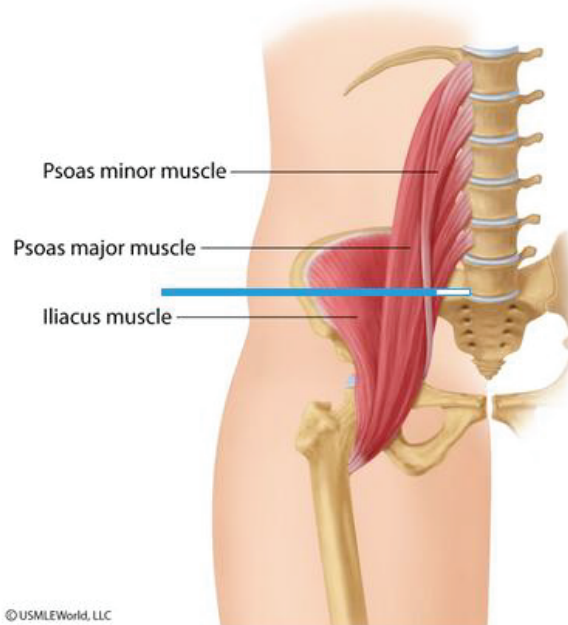
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Exhibit Display

The iliopsoas muscle



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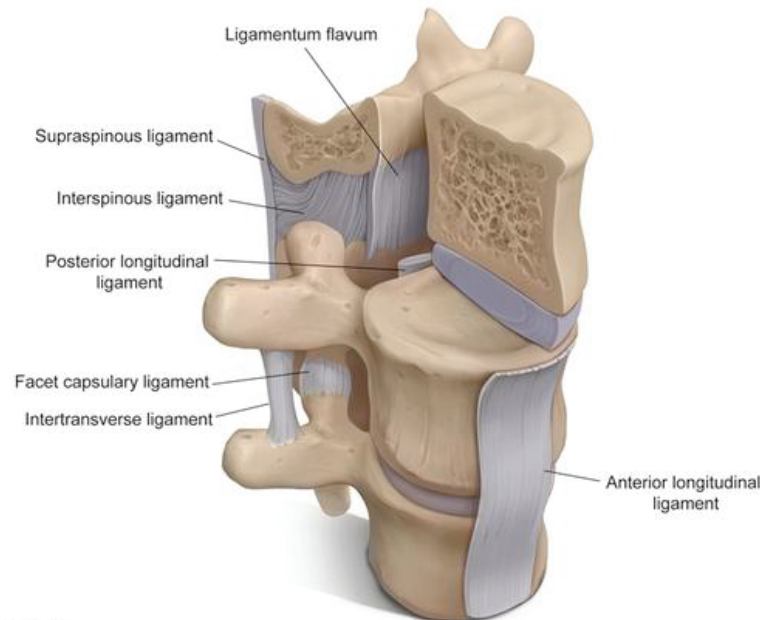
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Vertebral ligaments



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My Notebook





Patients often present subacutely with abdominal/pain, fever, and inguinal mass. HIV infection,

intravenous drug use, and diabetes mellitus are risk factors for primary psoas abscess development.

(Choice A) The erector spinae is a large muscle group of the back that courses longitudinally along the spinous processes. Bilateral contraction causes spine extension.

(Choice C) The **ligamenta flava** are paired elastic ligaments that connect the vertebral laminae. The ligamenta flava form the posterior wall of the spinal canal and help stabilize the spine.

(Choice E) The transversus abdominis (transversalis) muscle is the most internal of the **anterior abdominal wall muscles**. It lies immediately deep to the internal oblique and helps to flex the trunk as well as increase intraabdominal pressure during forced expiration.

Educational objective:

The psoas muscle originates from the anterior surface of the transverse processes and lateral surface of the vertebral bodies and functions primarily as a hip flexor. Psoas abscess may form due to direct spread of infection from an adjacent structure (eg, vertebral bodies, appendix, hip joint) or from hematogenous seeding from a distant site.

Anatomy

Rheumatology/Orthopedics & Sports

Psoas abscess

Subject

System

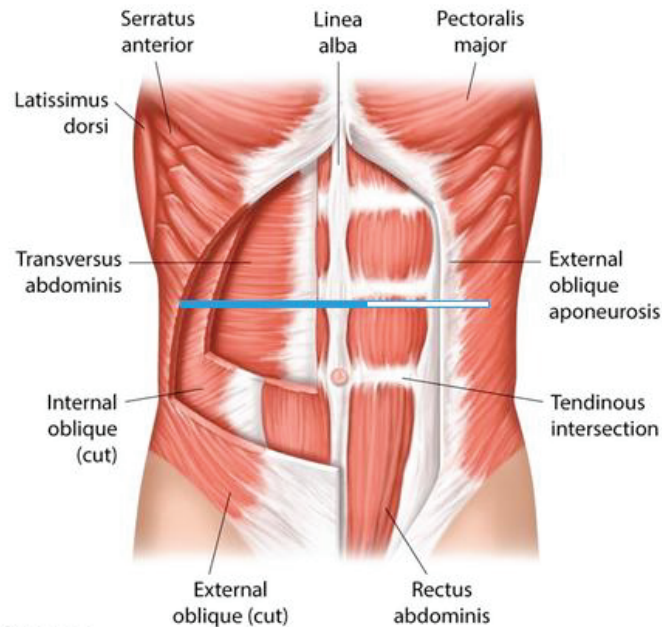
Topic



Patients often present subacutely with abdominal/ank pain, fever, and inguinal mass. HIV infection,

Exhibit Display

Abdominal wall musculature



Zoom In

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Reset

New | Existing

My Notebook

Subject

System

Topic

Block Time Remaining: 00:00:44

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Feedback

Suspend

End Block

1
2
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A 48-year-old woman comes to the office with a 4-month history of pain, stiffness, and swelling of her hands, feet, and knees that is associated with daily fatigue. She has taken over-the-counter nonsteroidal anti-inflammatory agents, but they only temporarily relieve the pain. The patient has no other medical issues. She does not use tobacco, alcohol, or illicit drugs and is not sexually active. Vital signs are within normal limits. BMI is 35 kg/m². The patient walks with a limp due to pain in the foot. There is symmetric swelling, tenderness, and restricted range of motion involving the wrists, ankles, forefeet, and knees. There is no skin rash. Laboratory studies show anemia. Which of the following is most likely to be the earliest finding during the development of this patient's condition?

- ☐ A. Fibrillation of articular cartilage
- ☐ B. Joint subluxation
- ☐ C. Marginal bone erosions
- ☐ D. Osteophyte formation
- ☐ E. Synovial neovascularization





hands, feet, and knees that is associated with daily fatigue. She has taken over-the-counter nonsteroidal anti-inflammatory agents, but they only temporarily relieve the pain. The patient has no other medical issues. She does not use tobacco, alcohol, or illicit drugs and is not sexually active. Vital signs are within normal limits. BMI is 35 kg/m². The patient walks with a limp due to pain in the foot. There is symmetric swelling, tenderness, and restricted range of motion involving the wrists, ankles, forefeet, and knees. There is no skin rash. Laboratory studies show anemia. Which of the following is most likely to be the earliest finding during the development of this patient's condition?

- ☐ A. Fibrillation of articular cartilage (26%)
- ☐ B. Joint subluxation (9%)
- ☐ C. Marginal bone erosions (19%)
- ☐ D. Osteophyte formation (13%)
- ☒ E. Synovial neovascularization (31%)

Correct

31%



01 min, 19 secs



03/13/2021

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End Block



Clinical features of rheumatoid arthritis

Clinical presentation

- Pain, swelling & morning stiffness in multiple joints
- **Small joints** (PIP, MCP, MTP); spares DIP joints
- Systemic symptoms (fever, weight loss, anemia)
- **Cervical spine** involvement: subluxation, cord compression

Laboratory/imaging studies

- Positive rheumatoid factor & **anti-CCP antibodies**
- C-reactive protein & ESR correlate with disease activity
- **X-ray**: soft tissue swelling, joint space narrowing, bony erosions

Anti-CCP = anti-cyclic citrullinated peptide; **DIP** = distal interphalangeal; **ESR** = erythrocyte sedimentation rate; **MCP** = metacarpophalangeal; **MTP** = metatarsophalangeal; **PIP** = proximal interphalangeal.

This patient has a chronic, symmetric, polyarticular arthritis with joint swelling and stiffness consistent with early **rheumatoid arthritis** (RA). RA is a progressive autoimmune disorder that is often associated with signs of systemic inflammation (eg, fatigue, fever, anemia). It has a peak incidence at age 50-75 but can





This patient has a chronic, symmetric, polyarticular arthritis with joint swelling and stiffness consistent with early **rheumatoid arthritis** (RA). RA is a progressive autoimmune disorder that is often associated with signs of systemic inflammation (eg, fatigue, fever, anemia). It has a peak incidence at age 50-75 but can occur at any age; women are affected more commonly than men.

The pathogenesis of RA begins with activation of T lymphocytes in response to rheumatoid antigens (eg, citrullinated peptides, type II collagen). Activated T cells release cytokines that cause **synovial hyperplasia** with recruitment of additional mononuclear cells. The accelerated metabolic rate of the inflamed synovial tissue leads to **local hypoxia** and increased production of hypoxia-inducible factor 1 and vascular endothelial growth factor by local macrophages and fibroblasts, resulting in **synovial angiogenesis** (neovascularization).

As the disease progresses, new blood vessels provide nutrients that facilitate expansion of inflamed synovium into a **rheumatoid pannus**, an invasive mass composed of fibroblast-like synovial cells, granulation tissue, and inflammatory cells. Over time, the pannus encroaches into the joint space and can destroy the articular cartilage and erode the underlying subchondral bone (**Choice C**). Ossification of the pannus can lead to fusion of the bones across the affected joint (bony ankylosis).

(Choices A and D) Osteoarthritis is characterized by progressive fibrillation (ie, fissuring, fracturing) and





pannus can lead to fusion of the bones across the affected joint (bony ankylosis).

(Choices A and D) Osteoarthritis is characterized by progressive fibrillation (ie, fissuring, fracturing) and erosion of articular cartilage due to increased biomechanical stress. Periarticular findings include osteophyte formation and subchondral sclerosis due to extensive bone remodelling. In contrast, RA is more frequently associated with periarticular bone erosions.

(Choice B) Late-stage RA is characterized by widespread joint deformities. Characteristic findings include ulnar deviation at the metacarpophalangeal joints, swan-neck deformities (hyperextension at the proximal interphalangeal joints with flexion at the distal interphalangeal joints) in the digits, and additional deformities (eg, volar subluxation of the carpus, radial drift) at the wrists.

Educational objective:

Rheumatoid arthritis is characterized by synovial hyperplasia with inflammatory infiltrates. The accelerated metabolic rate of the inflamed synovium causes local hypoxia, which leads to synovial angiogenesis. As the disease progresses, the joint space is replaced by a rheumatoid pannus (an invasive mass of fibroblast-like synovial cells, granulation tissue, and inflammatory cells) which can destroy the articular cartilage and underlying subchondral bone.

References



1
2
3
4
5



Item 3 of 5

Question Id: 11801



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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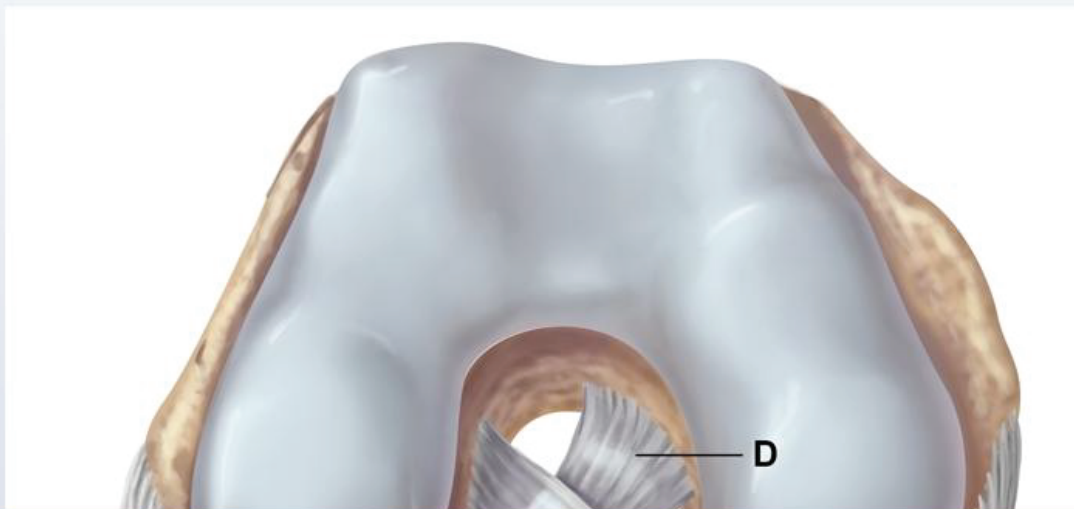


Text Zoom



Settings

A 16-year-old boy comes to the emergency department due to right knee pain after a fall. His symptoms started after a ski accident in which he twisted the right lower leg outward relative to the thigh. He has no medical conditions and currently takes no medications. On examination, there is swelling and tenderness on the medial aspect of the right knee. Widening of the medial joint line can be felt when a gentle force is applied to the lateral knee with the lower leg kept stationary. Which of the following labelled structures is most likely injured in this patient?



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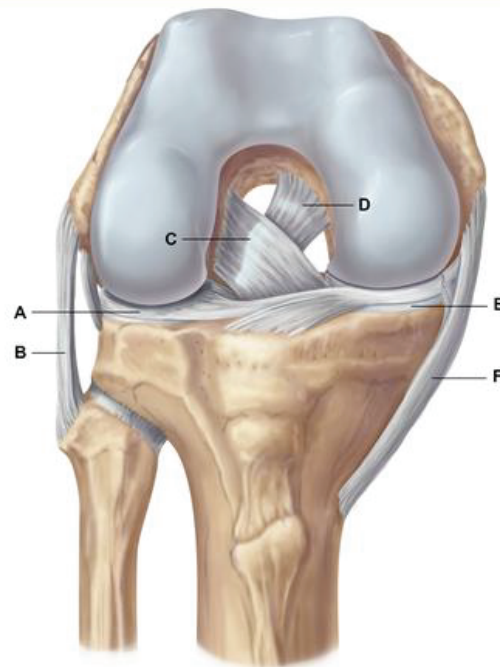


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2
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Item 3 of 5
Question Id: 11801



Previous

Next

Full Screen

Tutorial

Lab Values

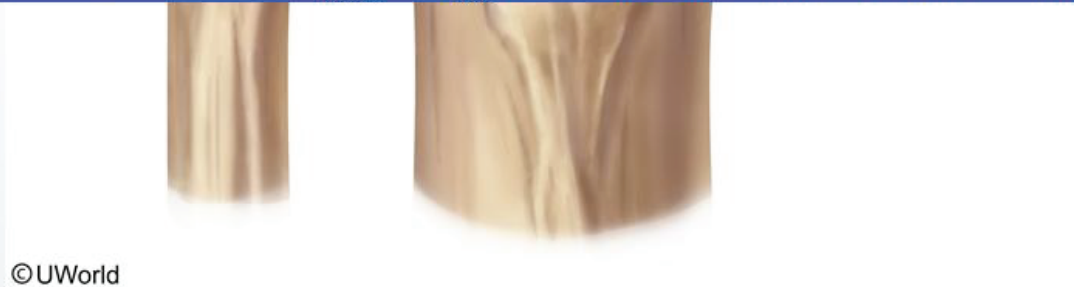
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- ☐ A.A
- ☐ B.B
- ☐ C.C
- ☐ D.D
- ☐ E.E
- ☐ F.F

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Feedback

Suspend

End Block

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Item 3 of 5

Question Id: 11801



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



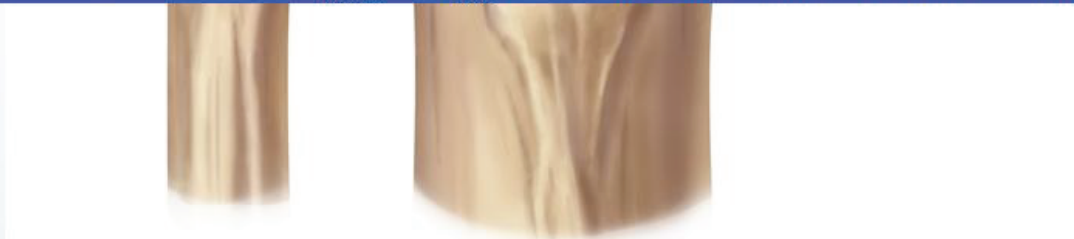
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- ☐ A. A (2%)
- ☐ B. B (10%)
- ☐ C. C (3%)
- ☐ D. D (1%)
- ☐ E. E (6%)
- ☒ F. F (75%)

Correct

75%

01 min, 01 sec

11/27/2020

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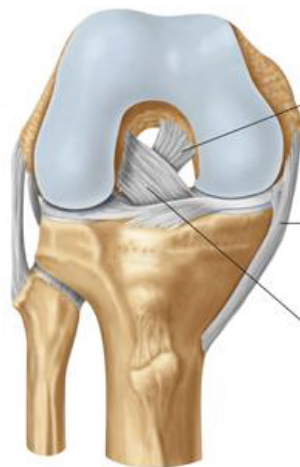
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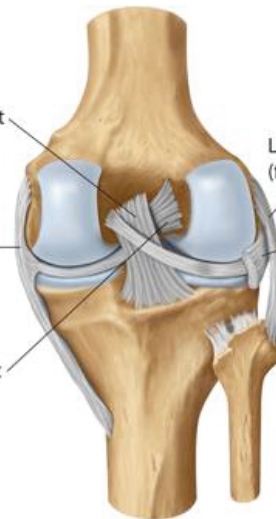
Exhibit Display

Anterior view



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Posterior view



Zoom In

Zoom Out

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This patient has an injury to the **medial collateral ligament** (MCL). The MCL attaches proximally to the medial epicondyle of the femur and resists forces that push the knee medially. MCL injury typically occurs after a twisting injury or blow to the lateral knee while the foot is planted (**valgus stress injury**).

The valgus stress test is performed with the knee extended by placing one hand along the lateral thigh and pressing inward while the other hand is placed on the medial aspect of the ankle and pushed outward. Laxity of the knee and/or medial joint line widening indicates MCL injury.

(Choices A and E) The lateral (A) and medial (E) menisci reduce shock and help transfer force from the upper to the lower leg. Medial meniscal injury can occur with twisting movement of the knee and often accompanies MCL injury. Lateral meniscal injury is less common. Meniscal injury is diagnosed by joint line tenderness while the knee is flexed.

(Choice B) The lateral collateral ligament (LCL) resists excessive lateral movement of the knee. LCL injury is uncommon but would be characterized by laxity of the knee with varus stress.

(Choice C) The anterior cruciate ligament (ACL) resists anterior movement and medial rotation of the tibia. Injury is indicated by increased anterior movement of the tibia in relation to the femur (eg, anterior





lateral movement of the knee is flexed.

(Choice B) The lateral collateral ligament (LCL) resists excessive lateral movement of the knee. LCL injury is uncommon but would be characterized by laxity of the knee with varus stress.

(Choice C) The anterior cruciate ligament (ACL) resists anterior movement and medial rotation of the tibia. Injury is indicated by increased anterior movement of the tibia in relation to the femur (eg, anterior drawer test, Lachman test).

(Choice D) The posterior cruciate ligament (PCL) stabilizes the tibia and femur during knee movement. Excessive backward movement of the tibia in relation to the femur (posterior drawer test) indicates PCL injury.

Educational objective:

The medial collateral ligament resists force that pushes the knee medially. Increased laxity of the knee with the valgus stress test indicates injury to the medial collateral ligament.

References

- [MCL injuries of the knee: current concepts review.](#)

Anatomy

Rheumatology/Orthopedics & Sports

Medial collateral ligament injury

Subject

System

Topic





A 72-year-old man comes to the primary care clinic with a 6-month history of back and bilateral thigh pain provoked by walking. He normally can walk only 2-3 blocks before having to stop due to pain. However, when he is out walking with his grandchild, leaning on the stroller seems to provide pain relief. The patient also notices an occasional tingling sensation in his lower extremities. He has no prior trauma or history of rheumatologic disorders. On physical examination, muscular strength is normal and the sensory findings are unremarkable. Peripheral pulses are full and symmetric. Thickening of which of the following ligaments is most likely contributing to this patient's current presentation?

- ☐ A. Anterior longitudinal
- ☐ B. Iliolumbar
- ☐ C. Interspinous
- ☐ D. Ligamentum flavum
- ☐ E. Sacroiliac

Submit

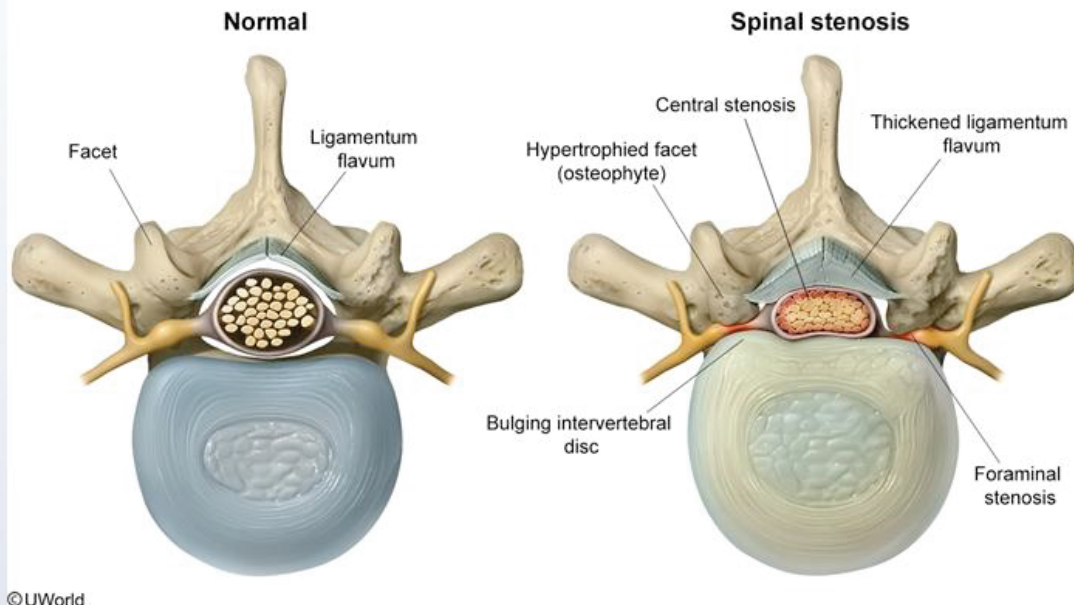


A 72-year-old man comes to the primary care clinic with a 6-month history of **back** and bilateral thigh pain provoked by walking. He normally can walk only 2-3 blocks before having to stop due to pain. However, when he is out walking with his grandchild, **leaning** on the stroller seems to provide pain relief. The patient also notices an occasional **tingling sensation** in his lower extremities. He has no prior trauma or history of rheumatologic disorders. On physical examination, muscular strength is normal and the sensory findings are unremarkable. Peripheral pulses are full and symmetric. Thickening of which of the following ligaments is most likely contributing to this patient's current presentation?

- ☐ A. Anterior longitudinal (10%)
- ☐ B. Iliolumbar (15%)
- ☐ C. Interspinous (11%)
- ☒ D. Ligamentum flavum (31%)
- ☐ E. Sacroiliac (30%)



Lumbar spinal stenosis



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This patient presents with **spinal stenosis**, an abnormal narrowing of the spinal canal occurring most commonly in the lumbar region. Compression of nerve roots results in a number of neurologic symptoms, including lower extremity pain, numbness/paresthesia, and weakness. The onset of pain with walking



This patient presents with **spinal stenosis**, an abnormal narrowing of the spinal canal occurring most commonly in the lumbar region. Compression of nerve roots results in a number of neurologic symptoms, including **lower extremity pain**, **numbness/paresthesia**, and **weakness**. The onset of pain with walking is referred to as "neurogenic claudication" as it may resemble symptoms seen in vascular claudication. However, the symptoms of spinal stenosis are **posture-dependent**. Extension of the lumbar spine (eg, standing, walking upright) further narrows the spinal canal and worsens the symptoms, whereas lumbar flexion (eg, walking uphill, [leaning on a stroller/shopping cart](#)) relieves the pain.

Degenerative arthritis of the spine is the most common cause of spinal stenosis, typically occurring in patients age >60. Over time, the intervertebral disc degenerates and begins to protrude, resulting in a corresponding loss in disc height. This loss of height places a disproportionate load on the posterior aspect of the spinal column, leading to formation of facet joint osteophytes and hypertrophy of the [ligamentum flavum](#) (a strong elastic ligament supporting the posterior aspect of the spinal canal). These physiologic changes lead to mechanical compression of nerve roots and corresponding neurologic symptoms.

(Choice A) The anterior longitudinal ligament covers the anterior aspect of the vertebral bodies, preventing excess spinal extension.

(Choice B) The iliolumbar ligament connects the fifth lumbar vertebrae to the iliac crest, strengthening the



1
2
3
4
5



Item 4 of 5

Question Id: 12073



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display

Shopping cart sign



Symptoms worsen
with lumbar extension

Leaning forward relieves
pressure, lessening symptoms

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Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:03:47

TUTOR

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Feedback

Suspend

End Block

1
2
3
4
5



Item 4 of 5

Question Id: 12073



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

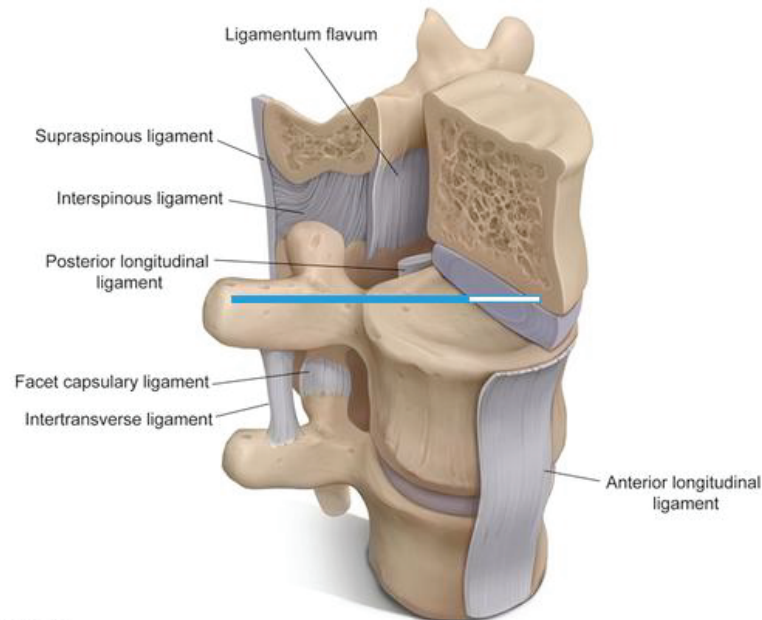
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Text Zoom

Settings

Exhibit Display

Vertebral ligaments



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Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:03:47

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Feedback

Suspend

End Block



(Choice A) The anterior longitudinal ligament covers the anterior aspect of the vertebral bodies, preventing excess spinal extension.

(Choice B) The iliolumbar ligament connects the fifth lumbar vertebrae to the iliac crest, strengthening the lumbosacral joint.

(Choice C) The interspinous ligaments connect the spinous processes and help limit flexion of the spine.

(Choice E) The sacroiliac ligament prevents distraction of the sacroiliac joint.

Educational objective:

Spinal stenosis occurs most commonly in the lumbar region and presents with posture-dependent lower extremity pain, numbness/paresthesia, and weakness. The most common cause is degenerative arthritis of the spine, which results in narrowing of the spinal canal due to intervertebral disc herniation, ligamentum flavum hypertrophy, and osteophyte formation affecting the facet joints.

References

- [Management of lumbar spinal stenosis.](#)

Anatomy

Subject

Rheumatology/Orthopedics & Sports

System

Spinal stenosis

Topic



1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 37-year-old woman is brought to the emergency department following a motor vehicle collision. She lost control of her car while going around a corner and struck a brick wall head on. The patient has severe pain at the right hip with any movement. Examination shows that the right lower extremity is adducted and internally rotated and appears shorter than the contralateral leg. Range of motion testing at the hip is limited in all directions due to severe pain. X-ray of the hip is shown in the [exhibit](#). Which of the following structures is most vulnerable to involvement from this patient's injury?

- ☐ A. Femoral artery
- ☐ B. Femoral nerve
- ☐ C. Lateral femoral cutaneous nerve
- ☐ D. Sciatic nerve
- ☐ E. Superior gluteal artery

Submit

Block Time Remaining: 00:03:48

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Feedback



Suspend



End Block

1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

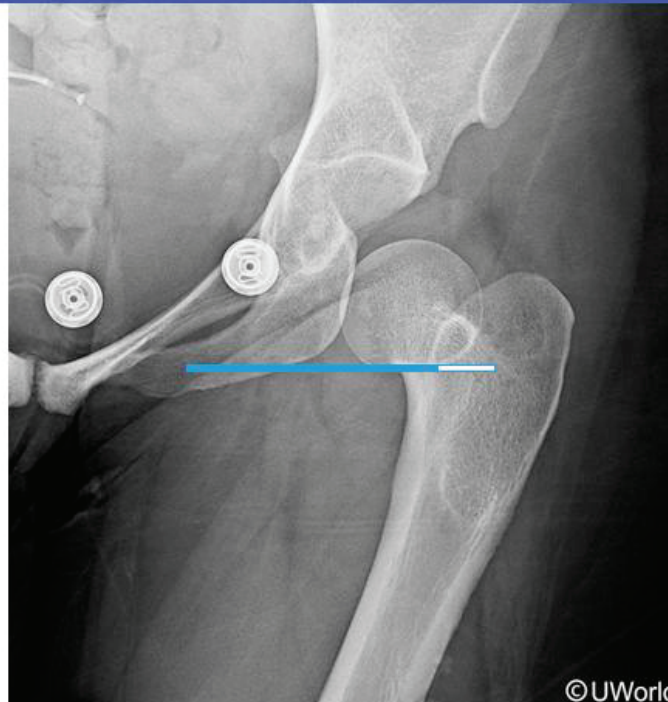
Calculator

Reverse Color

Text Zoom

Settings

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:03:53

TUTOR

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block

1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 37-year-old woman is brought to the emergency department following a **motor vehicle collision**. She lost control of her car while going around a corner and struck a brick wall head on. The patient has severe pain at the right hip with any movement. Examination shows that the right lower extremity is adducted and internally rotated and appears shorter than the contralateral leg. Range of motion testing at the hip is limited in all directions due to severe pain. X-ray of the hip is shown in the **exhibit**. Which of the following structures is most vulnerable to involvement from this patient's injury?

- ☐ A. Femoral artery (20%)
- ☐ B. Femoral nerve (16%)
- ☐ C. Lateral femoral cutaneous nerve (14%)
- ☒ D. Sciatic nerve (35%)
- ☐ E. Superior gluteal artery (14%)

Correct



35%
Answered correctly



51 secs
Time Spent



11/05/2020
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Block Time Remaining: 00:04:38
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Feedback

Suspend

End Block

1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



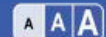
Notes



Calculator



Reverse Color



Text Zoom



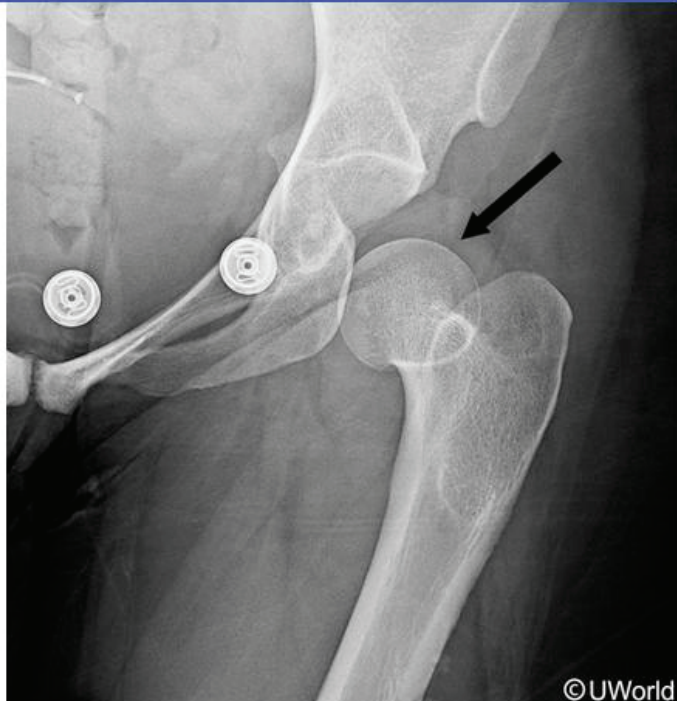
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Answered correctly

Time Spent

Last Updated

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:04:38

TUTOR

<https://t.me/USMLEWorldStep1>



1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient has a **posterior hip dislocation** (ie, femoral head displaced posteriorly from the acetabulum), which commonly occurs in head-on motor vehicle collisions in which the knee strikes the dashboard or from a fall in frail, elderly patients. The risk is increased with prosthetic joints.

On examination, the leg with a posterior hip dislocation appears **shortened** and **internally rotated**, with the hip held in **flexion and adduction**. Range of motion is limited and painful. Posterior dislocation can be mistaken for intertrochanteric hip fracture, which can also present with leg shortening; however, the leg is typically rotated externally with intertrochanteric fracture due to contraction of the psoas and iliacus without the normal acetabular counterforce.

The **sciatic nerve** runs **posterior to the hip joint** and is vulnerable to injury with posterior hip dislocation. Findings of sciatic injury include **weakness of ankle dorsiflexion**, decreased ankle reflex, and decreased sensation in the **distribution of the nerve**.

(Choices A and B) The femoral artery runs **anterior to the hip** and can be injured in anterior (not posterior) dislocation, which is rare and typically occurs in association with additional traumatic injuries (eg, hip fracture); examination shows abduction and external rotation of the thigh. The femoral nerve also runs **anterior to the hip joint**; it is occasionally injured in hip arthroplasty but is not at risk in posterior dislocation.

Block Time Remaining: 00:04:38

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Feedback



Suspend



End Block

1
2
3
4
5

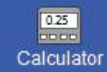
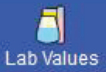
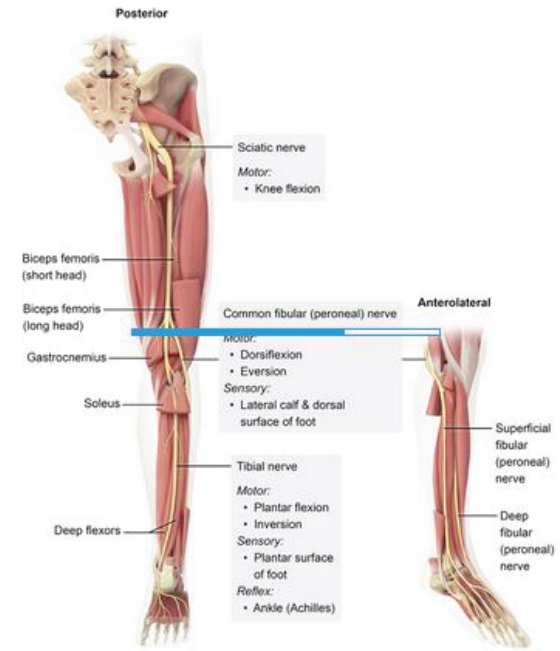


Exhibit Display

Sciatic nerve



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1
2
3
4
5

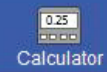
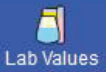


Exhibit Display

Sciatic nerve

| Motor function | Cutaneous innervation |
|--|---|
| Leg flexion at the knee (see also tibial & peroneal nerves) | <p>The diagram shows two views of a human leg. The left view is a posterior view with green shading on the back of the leg and foot. The right view is an anterior view with green shading on the front of the leg and foot. Labels with leader lines point to the following areas: Common peroneal (tibular) nerve (pointing to the front of the lower leg), Tibial nerve (pointing to the back of the lower leg), and Sural nerve (pointing to the outer side of the foot).</p> |

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1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

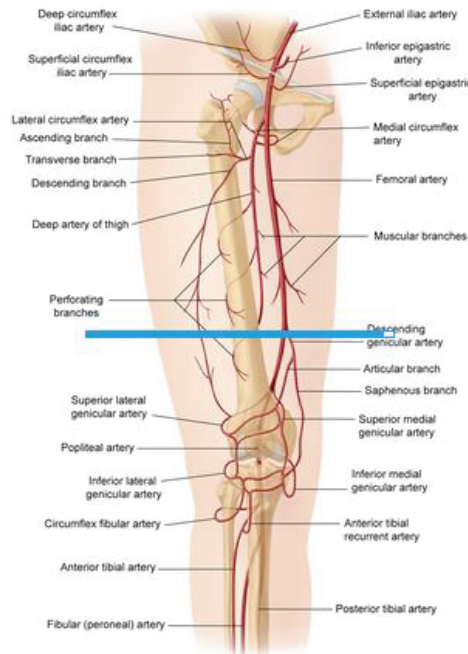
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Text Zoom

Settings

Exhibit Display

Arteries of anterior thigh and knee



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Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:04:38

TUTOR

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Feedback

Suspend

End Block

1
2
3
4
5



Item 5 of 5

Question Id: 18583



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

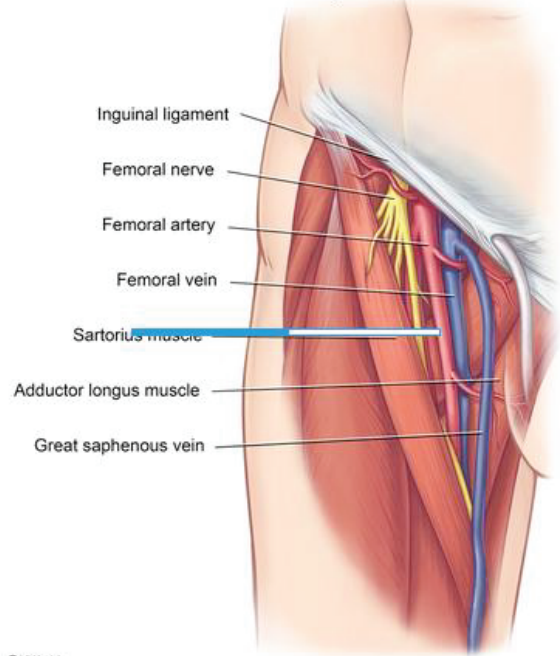
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Settings

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Femoral triangle



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New | Existing

My Notebook

Block Time Remaining: 00:04:38

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Feedback

Suspend

End Block

1
2
3
4
5



dislocation, which is rare and typically occurs in association with additional traumatic injuries (eg, hip fracture); examination shows abduction and external rotation of the thigh. The femoral nerve also runs **anterior to the hip joint**; it is occasionally injured in hip arthroplasty but is not at risk in posterior dislocation.

(Choice C) The lateral femoral cutaneous nerve passes **under the inguinal ligament** into the lateral thigh; it is vulnerable to external compression but is not at risk in hip dislocation.

(Choice E) The superior gluteal artery arises from the internal iliac artery in the **posterior pelvis** and can be injured in pelvic fracture. It does not approximate the hip joint and is not vulnerable in posterior dislocation.

Educational objective:

Posterior hip dislocation (ie, femoral head displaced posteriorly from the acetabulum) can occur in motor vehicle collisions in which the knee strikes the dashboard or from falls in elderly patients. On examination, the leg appears shortened and internally rotated, with the hip held in flexion and adduction. The sciatic nerve is vulnerable to injury in posterior hip dislocation.

Anatomy

Rheumatology/Orthopedics & Sports

Hip fracture

Subject

System

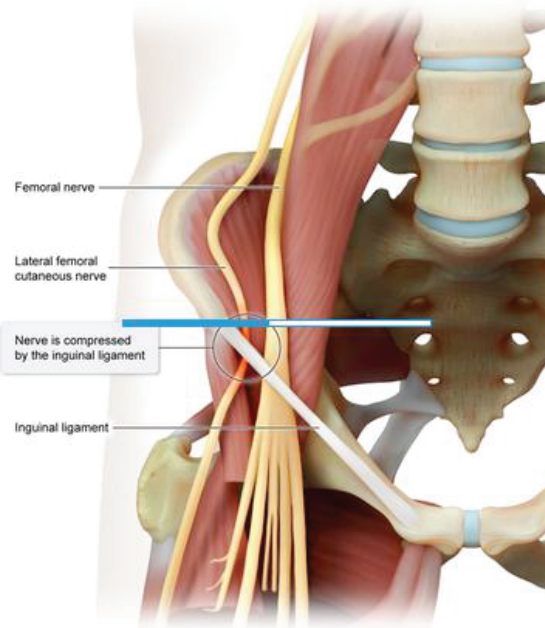
Topic



dislocation, which is rare and typically occurs in association with additional traumatic injuries (eg, hip

Exhibit Display

Lateral femoral cutaneous nerve & meralgia paresthetica



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Zoom Out

Reset

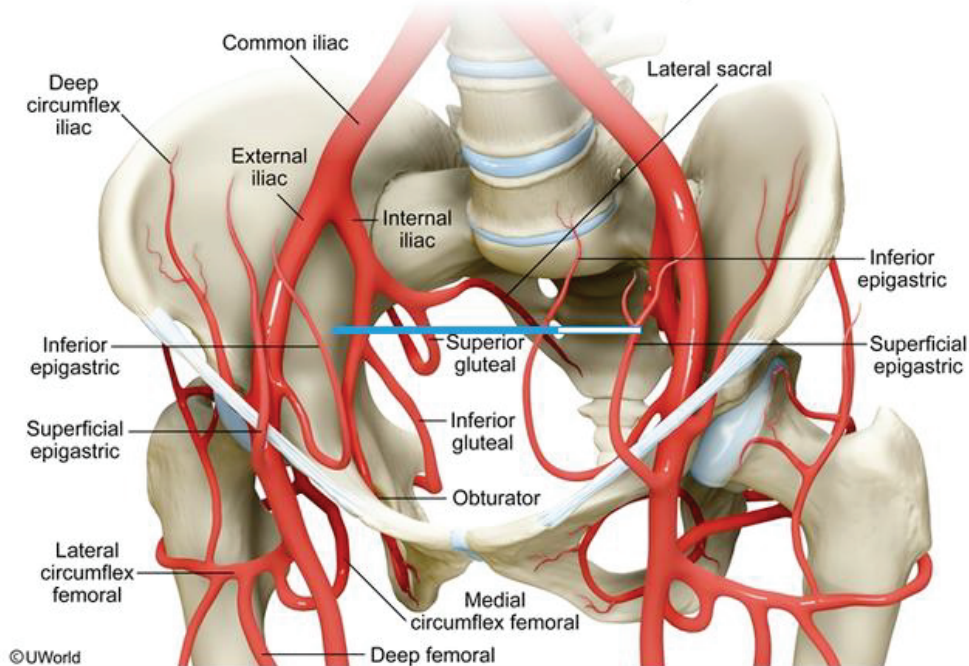
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dislocation, which is rare and typically occurs in association with additional traumatic injuries (eg, hip

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Branches of common iliac artery



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